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A PRELUDE TO ETHER ANESTHESIA*

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BALTIMORE

IN the thirteenth century Hugh of Lucca employed the *spongia somnifera* or sleeping sponge to relieve the pain of surgical operations. He is said to have introduced it in about 1250, a recent date in the history of anesthetics. Hugh's famous disciple, Theodoric (Teodorico Borgognoni, 1205–1296), Bishop of Cervia, described the sponge in his surgical treatise of 1266 and has sometimes been credited with its invention. References to it occur in the *Antidotarium* of Nicholas of Salerno, said to have been compiled in the eleventh century and one of the early medical books to be printed in the rich topography of Nicholas Jensen at Venice in 1471. Some authorities maintain that the prescription for the sponge was derived from older formulas for anodyne applications to the temples for insomnia and was used to produce a form of local anesthesia, citing references that appear in the works of Copho, Gaddesden and others. The celebrated remedy was prepared as follows:

> Take opium and juice of unripe mulberry, of hyoscyamus, of the juice of the leaves of the mandragora, of the juice of the wood ivy, of the juice of forest mulberry, of the seeds of lettuce, of the seed of the burdock, which has large and round apples, and of the water hemlock, each one ounce; mix the whole of these together in a brazen vessel, and then in it place a new sponge, and let the whole boil, and as long as the sun on dog days, till it (the sponge) consumes it all, and let it be boiled away in it. As often as there is need of it, place this same sponge into warm water for one hour, and let it be applied to the nostrils till he who is to be operated on has fallen asleep; and in this state let the operation be performed. When it is finished, in order to rouse him, place another dipped in vinegar, frequently to his nose, or let the juice of the roots of fenigreek be squirted into his nostrils. Presently he awakes.[1]

The use of a pain-nullifying agent, however, goes back to remote antiquity, for ever since man has suffered he has sought a "drowsy syrup" that might bring relief. Six thousand years ago and more, mandragora was employed by the Babylonians; there are references to soporifics in the Talmud; and in the twenty-first verse of the second chapter of *Genesis* we read: "And the Lord God caused a deep sleep to fall upon Adam, and he slept: and he took one of his ribs and closed up the flesh instead thereof." Indian hemp (*Cannabis indica*) was in all probability the drug used by the Egyptians when performing surgical operations, and it is claimed that Helen gave this same drug to Ulysses in the incident narrated in the *Odyssey*. The mention of bhang occurs in the *Arabian Nights*, and there is evidence that the Orientals and the Greeks were quite familiar with the narcotic properties of opium, henbane, dewtry, lettuce and hemlock.

Inhaling the vapor of bhang for anesthetic purposes is mentioned in the writings of Hippocrates about 400 B.C. and later references to some form of narcosis are to be found in the works of Pliny, Dioscorides, Paulus Aegineta, Celsus and Avicenna. Pliny the Elder (23–79 A.D.) described mandragora and spoke of its soporific powers. It was also recommended as a surgical sleeping draught by Dioscorides† and Apuleius.

About 165 A.D. the Greek physician and philosopher Galen employed as an anesthetic for the removal of teeth an application of "pirethrin root and strong vinegar, from the action of which, the remaining teeth may be preserved by covering them with a layer of wax. At the expiration of an hour, the tooth becomes so loosened, as to be easily removed."[2]

Hao Tho, Chinese court physician at the beginning of the third century, operated on his patients while they were under the influence of a preparation of the hemp plant sometimes called "may-yo" and similar to the hashish of the Arabs.

The Peruvian Indians found a remedy in coca leaves, chewing them and swallowing the saliva. Persisting in the habit, they were apparently able to build up a considerable immunity to pain. In 1911, H. J. Mozans[3] cited a modern instance of a *coquero* (one habitually chewing coca leaves) who was run over by a car. His foot was taken off in the accident, but he gave little or no evidence of suffering. The shamans or priests of old Peru also chewed

*This article forms the opening chapter of a forthcoming publication, *William Thomas Green Morton and the Discovery of Surgical Anesthesia*, by the late William W. Ford, M.D., D.P.H., emeritus professor of bacteriology, School of Hygiene and Public Health, Johns Hopkins University.

†Dioscorides was the first to refer to the use of mandragora wine as an anesthetic, and his formula was successfully tested by Richardson.[22]

the leaves and applied the spittle to the wounds of their surgical patients. From the active principle contained in the leaves of *Erythroxylon coca* the alkaloid cocaine was to be produced in the nineteenth century.

Compression effected by mechanical means and continued a sufficient length of time to cause numbness in that part of the body to be operated on, was first practiced by the Egyptians and has been reintroduced by surgeons at different periods.

Following Theodoric, Guy de Chauliac (1300–1368), the great surgeon of the Middle Ages, is the only medical historian of importance to mention or describe the "sleeping sponge."[4] In the medical writings of the period there are other references to the use of narcotics, chiefly opium, but at the same time the danger of asphyxia, congestions and even death as a result was emphasized. Unquestionably this did much to retard the practice of any extensive drugging in the treatment of patients. It is stated, however, that criminals of the fourteenth, fifteenth and sixteenth centuries, when facing execution or prolonged forms of torture, frequently had some narcotic dose administered by a compassionate jailer.

More than one reference to anesthesia has occurred in literature while the actual use of it was declining. Boccaccio, Shakespeare, Marlowe and Middleton all mention narcotics. The well-worn quotation:

> I'll imitate the pities of old surgeons
> To this lost limb, who, ere they show their art,
> Cast one asleep, then cut the diseased part.

taken from Middleton's *Women Beware Women*, furnishes perhaps the best example.

* * *

In the middle of the sixteenth century the skillful hands of Ambroise Paré (1510–1590) lessened the supreme torments of surgery by the application of ligatures and simple dressings in place of boiling oil or cauterization with red-hot irons—the usual treatment for wounds and the stumps of amputated limbs. Following on his chance discovery, as military surgeon before Turin, that gunshot wounds were not "poisonous," Paré opposed the doctrines of his contemporaries and conducted a spirited campaign for the adoption of soothing methods in wound treatment, but the use of the sleeping potion or "sponge" was apparently unknown to him. And in the seventeenth century, during which medical history was enriched by an imposing catalogue of names beginning with that of William Harvey (1578–1657) and the dignity of medicine was so ably portrayed in the canvases of some of the great Dutch painters, including the "Anatomies" of Adriaen Backer and Johan Van Neck, the employment of any pain-relieving agent was forgotten or almost wholly disregarded.

In 1730 the chemist Frobenius described sulfuric ether in the *Philosophical Transactions* of the Royal Society at London,[5] designating it "spiritus vini aethereus." The preparation of ether by the action of sulfuric acid on alcohol had been known since the thirteenth century. Raymond Lully (1235–1315), philosopher and alchemist of prominence, was apparently the first to discover it. The drug was then referred to as "sweet vitriol" or "*oleum dulce vitrioli*." In 1540 ether was rediscovered and its properties described by Valerius Cordus (1515–1544), a young apothecary and a student under Paracelsus, who had once happened on ether himself, it is stated, trying the effects of it on chickens. More than a century later "sweet vitriol" was also mentioned by Sir Isaac Newton, Godfrey and Boyle.

During the eighteenth century the medicinal employment of ether was alluded to by such prominent physicians as Hoffmann (Hoffmann's anodyne), Cullen, Alston, Lewis and the Monros. In 1795 Richard Pearson recommended the inhalation of ether in treating phthisis or pneumonia, directing that the patient "pour one or two teaspoonfuls of pure vitriolic ether, or ether impregnated with icuta . . . into a teacup or wineglass and inhale the same three, four or five times a day."[6] Several communications from Pearson are included in *Factitious Airs*,[7] the essays of James Watt and Dr. Beddoes, published at Bristol, England, in 1795, and printed in the *Annals of Medicine* the following year. One of Pearson's communications refers to a letter from Dr. Thornton describing the inhalation of sulfuric ether in treating catarrh, where the patient, much relieved, fell into a deep slumber.

In 1815 Nysten, in a dictionary of medical sciences,[8] spoke of ether as familiarly known for mitigating the pains of colic and other minor ills, and described apparatus or methods for inhaling it.

Michael Faraday, in 1818, published the following in the *Quarterly Journal of Science and the Arts*: "When the vapour of ether is mixed with common air and inhaled, it produces effects very similar to those occasioned by nitrous oxide. By the incautious breathing of ether vapour, a man was thrown into a lethargic condition which, with a few interruptions, lasted for thirty hours."

Dr. John Collins Warren spoke of resorting to the inhalation of ether as early as 1805 in order to relieve a patient dying of pulmonary tuberculosis.[9] In 1832 Daniel Drake listed ether among the remedies to be taken internally for cholera.[10] Franklin Bache, in 1833, collaborating in the preparation of the massive *United States Dispensatory* (first edition) gave a description of the chemical properties of the drug and referred to its medicinal uses.[11] Other American authorities mentioning ether during the decade of 1822–1832 included Godman, Mitchell and Professor Samuel Jackson. In considering the early references, however, it should be remembered

that the chemistry of the various substances called "ether" was not always well understood. Accurate directions for making it were probably first given in the *Pharmacopoeia* published by the Massachusetts Medical Society in 1808 and prepared for the Society by Dr. Jacob Bigelow and Dr. James Jackson. But it was not until 1830 that methods of preparing ether were given *in extenso* and became widely available in America. In that year the *Pharmacopoeia of the United States* gave a complete account of the preparation of its listed drugs, and the chemistry of the different ethers was further cleared up when Daniel B. Smith[12] published a comprehensive paper in the *Journal of the Philadelphia College of Pharmacy* for 1832–1833. He described over fourteen chemical compounds called "ether," among them a variety of chloric ether (later known as chloroform), sulfuric ether and oil of wine.*

Additional references to ether appeared in Pereira's widely read *Elements of Materia Medica*,[13] published in 1839—three years before the first operation under ether narcosis was to be performed by a young country practitioner at Jefferson, Georgia.

Earlier and painstaking investigation, which Sir Clifford Allbutt styled "the pathetic quest for oxygen," terminated brilliantly with the discovery of several gases in the second half of the eighteenth century, and the Chemical Age was firmly established. The discovery of carbon dioxide by the Scottish chemist Joseph Black, in 1757, was followed by the discovery within the next eighteen years of hydrogen by Cavendish, nitrogen by Rutherford and oxygen by Priestley, the Swedish investigator Scheele and Lavoisier. Preceding his discovery of "dephlogisticated air," as he called oxygen in accordance with Stahl's doctrine,† Joseph Priestley had discovered nitrous oxide in 1772. In 1775 oxygen, which John Mayow had come so near discovering in the seventeenth century, was once more isolated and clearly defined by Antoine-Laurent Lavoisier, and the phlogistic doctrine, long confusing and hampering chemists, was overthrown by this distinguished worker.

Medical practice was soon influenced by the various discoveries, particularly that of oxygen, "physicians were carried away by their imaginations to the extent of attributing diseases either to lack or excess of oxygen, or to some fine-spun modifications of this theory," as Garrison[14] has said.

A pioneer in the use of gases in medicine and contributing indirectly to the advancement of anesthesia was Dr. Thomas Beddoes, who founded a Pneumatic Institute at Clifton Hotwells near Bristol, England, in 1798. Here bodily and mental ills were treated by the inhalation of gases, and a sort of inhalation therapy developed and became extremely popular for a time.

The noted James Watt, in addition to collaborating with Beddoes in the publication of *Factitious Airs*, which related to the pneumatic methods, had constructed the apparatus at the institute, and Humphry Davy was Beddoes's chief assistant. In 1799 Davy[15] published the results of his experiments with nitrous oxide gas, which he had discovered to be an anesthetic while inhaling it to relieve an aching tooth. A little later he gave a series of popular lectures, followed by demonstrations of nitrous oxide, calling it "laughing gas." In 1800 further demonstrations of the gas were given by William Allen, the lecturer on chemistry at Guy's Hospital in London.

A man of wide interests and extensive acquaintance, Dr. Beddoes's work at Clifton, which the youthful Davy described as "the loveliest spot in the world," attracted the attention of Erasmus Darwin, Thomas Wedgewood, Wordsworth, Coleridge, Southey and many others. Both Southey and Coleridge were among the first to inhale nitrous oxide after Davy's successful experiments, Coleridge writing a glowing account of his sensations. But after a few years the initial enthusiasm began to decline, medical opinion altered, and there were many rumors concerning patients who had been troubled with dizziness, lowered pulse and other unfavorable symptoms as a result of pneumatic methods. Several years before his death in 1808, Beddoes, disillusioned, his theories having encountered strong opposition on all sides, converted the institute into a hospital where the usual forms of treatment were adopted, Humphry Davy meanwhile dropping his own investigation of nitrous oxide gas to win many laurels in other fields.

In about 1784 James Moore revived anesthesia by compression. The principal nerves and vessels of the neck were compressed to produce local anesthesia or insensibility. But after some fatal results this practice was soon discontinued.

Shortly before the French Revolution, Frederick Anton Mesmer employed animal magnetism or "magnetic emanations" to produce insensibility to pain, his armamentarium including a lilac robe (which he always wore at his hypnotic séances), a harmonica, a magnetized wand and later the *baquet* or wooden tub, containing a series of bottles "charged with animal magnetism." Discredited in Vienna, Mesmer had settled in Paris in 1786. Here he was also rebuffed, but not before he had enjoyed a period of extraordinary success and prosperity, being acclaimed by members of the French Court and other celebrities. He failed in all his efforts to obtain scientific recognition, however, and at the outbreak

*Until the early 1850's ether was produced by the open fire, intermittent distillation method. This method was not only dangerous from the standpoint of fire hazard but involved the problem of selecting the correct proportion of the distillate to be employed for anesthesia. In 1856 an important contribution was made by Edward R. Squibb, then assistant director at the United States Naval Laboratory. Experienced in the manufacture of ether for some years past, he had developed a method of making the drug by continuous steam heat through lead coils, and in an article entitled "Apparatus for the preparation of ether by steam," published in the September, 1856, issue of the *American Journal of Pharmacy*, gave a detailed report of his new, and revolutionary method.

†The principle of inflammability supposedly existing in combustible bodies. The theory was that when matter burns it gives off a hypothetical substance, "phlogiston."

of the Revolution left Paris and lived in retirement for some years before his death, which occurred in 1815. But mesmerism, invading surgery in the nineteenth century, was to have such disciples as Braid, the outstanding pioneer of scientific hypnosis and originator of "Braidism," Elliotson and Esdaile. John Elliotson, a friend of Thackeray's, to whom the novelist dedicated his *Pendennis*, performed the first surgical operations in about 1840 on patients who had been hypnotized, claiming success. In 1843 he published a pamphlet, *Numerous Cases of Surgical Operations without Pain in the Mesmeric State*, which soon provoked dispute and led to his resignation as president of the Royal Medical and Chirurgical Society, as a professor of practice in the University of London and to his withdrawal from other offices. James Esdaile fared much better in the Indian Medical Service, and his operative work among the Hindus, which he began in 1845, attracted attention for some time, although the general verdict of the Western scientific world was distinctly unfavorable.

In 1808, Frederich Wilhelm Sertürner, a German apothecary, extracted morphine from crude opium. Publishing the results of long experiment, he received honorary degrees from the Universities of Paris, St. Petersburg and Berlin, among others. In 1831, he was awarded a Montyon prize of 2000 francs for his discovery. Nevertheless, the conquest of pain in surgery was generally regarded as a remote possibility at this time, and Sertürner, becoming embittered by certain manifestations of professional jealousy, engaged at length in the study and improvement of firearms.

Severino had produced local anesthesia with snow and ice in 1640. At the battle of Eylau in February, 1807, Napoleon's surgeon-in-chief, Dominique Jean Larrey, who on occasion performed two hundred amputations in twenty-four hours, observed that wounded men half frozen from the cold experienced little pain when operated on. Larrey's discovery led to refrigeration anesthesia, which was shown to have so many undesirable features that it was soon abandoned. Later it was reintroduced.

In 1824 a young English physician, Henry Hill Hickman, performed a number of operations on animals, using carbon dioxide as an anesthetic. Hickman, it is said, first became interested in gases as a result of practicing for a time at Shiffnal, the birthplace of Dr. Beddoes. Returning to his native Ludlow in Shropshire, Hickman studied the work of Priestley, Davy and Faraday and conducted a series of experiments. Encouraged by the apparent success of his efforts, he went on to employ nitrous oxide when performing various operations on dogs, chickens and cats, and at about this time attempted to interest the Royal Society in his work. Writing to a friend, T. A. Knight, a botanist and member of the society, he gave a detailed report of his experiments, making the request that it be submitted to the proper authorities. But Knight, although at once interesting himself in the matter, was unable to help him. Both Sir Humphry Davy, then president of the Royal Society, and Michael Faraday were engaged in other absorbing problems, and Hickman's report was never even read before a committee.

Hickman, entertaining high hopes of being able to operate on his own patients under anesthesia, was not ready to accept defeat and printed a public letter. When this was ignored he presented a memorial to King Charles X of France in 1828, containing the statement: "It appears demonstrable that the hitherto most agonizing dangerous and delicate surgical operations may now be performed, with perfect safety, and exemption from pain, on brute animals in a state of suspended animation . . . ."[16] But the French were not interested after the Royal Academy of Medicine, with the possible exception of Dominique Larrey, failed to find anything of importance in Hickman's claims. Doomed to disappointment, Hickman could only continue his work alone. He died in 1830 at the age of twenty-nine, and more than a decade was to pass before the discovery of surgical anesthesia.

Samuel Guthrie, of Sackett's Harbor, New York, made chloroform in 1831 by distilling alcohol with chlorinated lime. In that same year chloroform was discovered independently by Soubeiran[17] in France, and Leibig[18] in Germany. It was first used medicinally as a solution of chloric ether, and regarded as a particularly pleasant intoxicant. "During the last six months, a great number of persons have drunk of the solution . . . in my laboratory," Guthrie wrote, "not only freely but frequently to the point of intoxication . . . it has appeared to be singularly grateful, both to the palate and stomach, producing promptly a lively flow of animal spirits, and consequent loquacity; and leaving, after its operation, little of that depression consequent to the use of ardent spirits."[19] In July, 1832, Daniel Smith, in classifying it among the ethers, observed: "The action of this ether on the living system is interesting and may hereafter render it an object of importance in commerce. Its flavor is delicious, and its intoxicating qualities equal to or surpassing those of alcohol."[12] Jean-Baptiste Dumas analyzed the solution in 1834 and gave it the name of chloroform, but its anesthetic qualities were not to be recognized until James Y. Simpson introduced it in childbirth some thirteen years later.

The picture, then, was not too bright. Surgical technics had improved since Paré, but human suffering was much the same. "A humiliating spectacle of the futility of science," John Hunter declared in the eighteenth century, and in the nineteenth Charles Darwin, writing his *Autobiographical Recollections*, recorded: "I also attended on two occasions the operating theatre in the hospital at Edinburgh and saw two very bad operations, one on a child,

but I rushed away before they were completed. Nor did I ever attend again."

Bleeding a patient to the point of unconsciousness had been advocated at different periods, and a large dose of alcohol to induce muscular relaxation and help to relieve the pain of surgical procedures was a common remedy in the nineteenth century, as it had been through many centuries. Some form of opium was also employed, but a lithotomy or amputation had still to be performed with lightning speed. "Keen pain is usually felt on tying the ligature," Nathan R. Smith[20] wrote concisely, and the professional attitude in general was probably expressed when Velpeau stated: "To escape pain in surgical operations is a chimera which we are not permitted to look for in our days. A cutting instrument and pain in operative medicine are two ideas which never present themselves separately to the mind of the patient, and it is necessary for us surgeons to admit their association."[21]

Yet even as Velpeau was putting his famous statement on paper a new chapter in medical history—one of unrivaled importance—was in preparation.

Through the thirties and forties of the last century itinerant chemical lecturers* in America were extending the practice, long known in medical schools, of sniffing ether or inhaling nitrous oxide gas. This practice was also in vogue among many of the students in the high schools or academies. Dr. Lewis H. Steiner (father of the late Dr. Walter R. Steiner of Hartford, Connecticut) graduated from the University of Pennsylvania in 1849. In his graduation thesis he gave an interesting account of the physiologic effects of sulfuric ether, and referred to the custom of some of the country boys of twenty years before, who would procure a bladder and a bottle of ether, inhaling the anesthetic as a regular form of diversion.

The chemical lecturer with his portable laboratory and his flow of words was a welcome visitor in communities that offered little or no entertainment, and where the effects of inhalation were unknown his demonstrations often led to the young people arranging a series of parties. Inhalation parties were hilarious occasions when, their clinical potentialities undreamt of, ether or nitrous oxide was inhaled to the point of intoxication, and singing, dancing and varieties of clowning were indulged in.

Perhaps at the height of their popularity the demonstrations led to the discovery—within four short years—of ether as an anesthetic by Dr. Crawford Williamson Long in 1842, the discovery of the anesthetic properties of nitrous oxide gas by Horace Wells in 1844, to be followed by the independent discovery and introduction of ether anesthesia by William Thomas Green Morton in 1846.

*These were the palmy days of the itinerants, and among those in medicine may be noted a group of "eye doctors" who appeared principally in New England or rural New York. In 1840 one of the doctors held clinics at Pompey, New York, the birthplace of Chapin A. Harris. Children with conjunctivitis, then a common affliction in the country districts, were taken to the clinics, where silver nitrate sticks were rubbed on the conjunctiva of the eyelids. Little was known of the danger of such a practice, in that too severe an application of silver nitrate would produce corneal opacity, and some of the children undergoing treatment developed partial blindness as a result.

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AIDS TO VISUAL EDUCATION IN MEDICINE

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BOSTON

THERE is greater need for a wide use of visual aids in teaching medical subjects at this time than there has been for many years. With such a large number of instructors now in the armed forces, it becomes necessary to use every possible aid in teaching.

Visual aids may take several forms. Large charts, photographs, lantern slides and motion pictures are all most necessary. Each of these forms has its own particular function to fulfill. It should be borne in mind that a photograph can tell a student more than can many pages of printed matter. Tests conducted by the United States Bureau of Education[1] have definitely proved that students learn more in a shorter time through pictures than they do from printed matter or the spoken word. With the greatly concentrated medical teaching program now in progress, it seems necessary to use all these visual aids to the largest possible extent.

Large charts are frequently advantageous in presenting material in tabulated form. They may be hand-lettered on large sheets of paper and placed on an easel before the students. These charts are of particular value if the students are required to copy the material in notebooks. The chart is usually left on the easel for a length of time sufficient to allow the slowest student to copy the material. Sufficient classroom lights should be on to enable the students to see their notebooks. Tests should be conducted to make sure that too much material is not placed on the charts. The material should be condensed as much as possible, bearing in mind that students absorb more readily two charts with ten lines on each than one chart with twenty lines. All charts must be so constructed that they can be easily read by students in the back rows.

Photographs can frequently be used to their best advantage in bedside teaching by showing the patient before and after treatment. They may also be enlarged and used as an exhibit. An exhibit of this kind is of no value unless a printed description accompanies each photograph and the students are given sufficient time in which to study it thoroughly. A place for a permanent exhibit can sometimes be arranged, with great benefit to the students.

The primary use of photographs is in the clinical record. It must always be borne in mind that the medical student rarely has a chance to see more than a small percentage of the patients both before and after they have been treated. The more complete the photographic record, the more valuable it will be for the purpose of study.

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Lantern slides are invaluable for covering a complete topic. They have been used and misused for many years, and there is a great deal of controversy over the best method of displaying them. It is generally understood that about forty lantern slides an hour is the maximum that can be taken in by students. This allows an average of somewhat over a minute for discussion of each lantern slide. If it is thought that more slides than this must be used, it is suggested that the slides be re-examined with a view toward discarding those that are of least importance. If more than forty lantern slides an hour are projected, the effect is most disconcerting to the student, sometimes to such a point that he gains nothing from the material. Many slides contain tabulated material — sometimes large quantities of it. From the student's point of view, this is undesirable, for two reasons. First, he is discouraged by a large mass of material and frequently does not bother to read it all. Second, large masses of printed material reproduced on a lantern slide are extremely small even when projected, and if the lecture room is large, those at the rear of the room may be unable to read what is on the screen. Some years ago the members of the Mayo Clinic[2] after considerable study reached the conclusion that for general use under varying conditions, fifteen typed lines of tabulated material is the maximum that should appear on a slide. This amount can be somewhat increased, probably to twenty lines, if the material is made with lettering guides instead of on a typewriter. Because of unknown projection conditions, such as the distance from the projector to the screen and the size of the screen in relation to that of the room, lantern slides must be so made that they will give the desired message regardless of local conditions.

Sometimes large quantities of material are necessarily projected on the screen to show the pattern or course of some particular subject; this does no harm. At other times a large amount of material is prepared in the form of a lantern slide as a guide to the lecturer. This is rather unfair to the student because the material must be read by the instructor and could be included in his text. If typed tabulated material is divided into sections with India ink, it becomes much easier to follow on the screen. Frequently masses of material can be broken down into more than one lantern slide with great benefit to the student. The instructor often loses sight of the fact that if his material is not good or is poorly presented, the student gains little or nothing from the time and effort that have been devoted to it by

the instructor. In the last analysis the material is being presented to the student for purposes of instruction, and if he gains nothing from it, it should be revised to the point where it is beneficial.

The next question is whether it is better to use typewritten material or that turned out by any of the semimechanical lettering guides now in use. Typewritten material is the poorest of all from the standpoint of projection on a screen because of the thin body of the characters and the ragged appearance of the type when enlarged on the screen. It is generally agreed that semimechanically lettered charts of tabulated material are much more easily read and present a much neater appearance. This is particularly important when material is to be presented at a medical meeting, because every speaker falls in the estimation of his audience if his lantern slides are poor.

When tabulated material is being prepared, more pleasing results will be gained if it is kept within proportions of the lantern slide, which is 3¼ by 4 inches. This produces the maximum size of letters on the screen for any given projection distance and ensures a minimum of wasted space.

Another subject of controversy has frequently been the number of x-ray films or ordinary photographs that can be reproduced on a single lantern slide. Here again, it depends somewhat on the subject whether more than two images can be placed on one slide and projected so that the entire audience can see the subject plainly. A single tiny spot on a chest plate reproduced in four films on one lantern slide is apt to show up poorly because of the small size of the projected image. On the other hand, details that are relatively large in a single film or photograph show up well in a number of images on one slide.

Motion pictures have come into great prominence during the last few years as a medium of teaching medicine. An enormous number of films have been made by many persons — some of them good and some worthless, not from the standpoint of poor photography but from that of scene length and continuity. This defect is caused by lack of preparation before the film is made. A good teaching film must be prepared in the form of a scenario or scene schedule. If it is an operative film, the photographer should see a similar operation before attempting to produce a motion picture, in order that he may know what to expect during the actual making of the film.

It is not infrequent that some interesting material is discovered during an operation and someone conceives the idea of having a motion picture made of it on the spur of the moment. Often after the film is made, it is never used and is forgotten, but if used by someone, it is found that the film was started in the middle of the operation. There is no preliminary matter to explain what went on before and no follow-up to show the end result. In general, films of this nature have absolutely no reason for being.

The preparation of a properly made medical teaching film begins with a conference between the instructor and the photographer, at which time a rough outline of what should be covered is laid out, and from this a taking schedule or scenario is made up. At that time the photographer and the instructor find out what each will need for material and what material will be required for each scene. They decide how much should be included in the scene, and whether to employ a close-up view or a long shot, and attend to the thousand and one details that must be settled before a single foot of film is run through the camera. In this way a minimum of material is wasted, the work proceeds more rapidly, and the end result is usually satisfactory and does not require additional scenes to be supplied at a later date.

When using color film in motion pictures, it is desirable that all the film be processed at one time, because there are minor variations in color in different processing solutions. For this reason the scene schedule should be complete before the film is processed. The use of color in motion pictures has been greatly accelerated in the last three years. Many medical subjects are far more realistic when done in color. Others can of course be done in black and white, but color is here to stay and wider use should be made of it whenever possible.

There has been much controversy over the length of a teaching film. Some experiences lead one to believe that a medical student cannot possibly stay awake through a film that lasts over ten minutes. Actually, if a film is presented in an interesting manner, there is little difficulty in keeping his attention. Thirty to forty minutes of running time seems to be the average period during which his interest can be held. Students frequently criticize motion pictures showing treatment because the latter is made to appear much too easy or simple. One of the reasons for this is that the average motion picture of treatment procedure shows only the high lights, omitting the minor motions and the preparation for treatment. On the other hand, if a film is to show all the preparation, treatment and aftercare, great pains must be taken so that it will not drag, for the student frequently loses interest if this occurs.

Four or five years ago, a noted pediatrician and a clinical photographer successfully worked out a method of presentation of motion pictures in conjunction with one of the former's lectures. The projection material consisted of a series of short films pertinent to the subject of the lecture, which were connected by short pieces of blank film. The running of each section required from 30 to 60 seconds. The instructor proceeded with his lecture, and at certain points he paused and a section of the film was shown. As soon as this particular section

had been run through the projector, the latter was stopped and the lecture proceeded until the next of what were called "punch points" was presented. In this way the student was able to see the actual characteristics of the subject under discussion at the time when the symptoms and treatment were fresh in his mind.

If the instructor depends on living patients to illustrate his lecture, he frequently finds that, when the lecture period comes around, he has no patient with the particular feature that he is going to discuss. By using motion pictures the subject is always there, rolled on a little reel and sealed in a tin. A much wider use of motion pictures could be made of a patient that could not be recorded photographically was the plantar aspect of the feet when bearing weight. It is now possible to do this quite successfully.[6] The required apparatus is simple and easily constructed. It opens a new field to the orthopedist for the photographic and visual record of patients with foot deformities.

Photography in the operating room is of great value in visual education, particularly when teaching time is so precious and students have little opportunity to observe operations. The photographic problems involved do not properly concern the instructor, and they vary in every hospital. Most of these have been solved, and a much greater

Focus of Lens in Inches	DISTANCE FROM SCREEN, IN FEET																	
	4	5	6	8	10	15	20	25	30	40	50	60	70	80	90	100	110	120
4¼	2.6	3.3	4.0	5.4	6.8	10.3	13.8											
5½	1.9	2.2	3.0	4.1	5.2	7.9	10.6	13.4										
6½	1.6	2.0	2.5	3.4	4.4	6.7	9.0	11.3	13.6									
8	1.3	1.6	2.0	2.7	3.5	5.4	7.2	9.1	11.0	14.8								
8½	1.2	1.5	1.9	2.6	3.3	5.1	6.8	8.6	10.3	13.9								
10		1.3	1.6	2.2	2.8	4.2	5.8	7.3	8.8	11.8	14.8							
12			1.3	1.8	2.3	3.5	4.8	6.0	7.3	9.8	12.3	14.8						
14			1.0	1.5	1.9	3.0	4.0	5.1	6.2	8.3	10.5	12.6	14.8					
16				1.3	1.6	2.6	3.5	4.5	5.4	7.3	9.1	11.0	12.9	14.8				
18				1.1	1.4	2.3	3.1	3.9	4.8	6.4	8.1	9.7	11.4	13.1	14.7			
20	Width of Screen Picture in Feet					2.0	2.8	3.5	4.3	5.7	7.3	8.8	10.2	11.8	13.2	14.8		
22						1.8	2.5	3.2	3.8	5.2	6.6	7.9	9.3	10.7	12.0	13.4	14.8	
24						1.6	2.2	2.9	3.5	4.7	6.0	7.2	8.5	9.7	11.0	12.3	13.5	14.8

Courtesy of the Spencer Lens Company

FIGURE 1. *Data on Lantern Slide Projection.*

in teaching medical subjects. It is claimed that they are too expensive, but if the medical student gets more instruction through the judicious use of motion pictures than from stills, the expense involved is immaterial. If a lecture is not worth the outlay of a sum of money to make it of greater value to the student, it is evidently of no great importance.

At the Children's Hospital a number of aids to better visual education have been developed. Some years ago a screen grid was superimposed on certain orthopedic photographs.[3, 4] With the aid of this grid it is possible to see the deviation from normal of a spine, the tilt of the head in torticollis, the bowing of the legs, asymmetry of the face and so forth. In short, the grid shows up any deviation from the normal. It has had wide use since it was first constructed. Also introduced is so-called "phantom photography," which is a controlled method of double exposure to show the range of mobility in a part.[5] This is also used effectively by the Orthopedic Department.

About two years ago it seemed that from the orthopedist's point of view the only external part employment of operative pictures could be made with profit to both the instructor and the student.

For pathologists, a new method of illumination of gross pathologic specimens was instituted a few years ago.[7] This method shows the surface texture of fresh specimens, whereas the older methods produced what might be called a "photographic map." Color photography of fresh specimens is often far superior to black-and-white photographs of the same specimen.

Infrared photography can sometimes be used to advantage. It must be remembered that infrared light picks up anything blue, such as veins, and makes it plainly visible if it lies near the skin surface, whereas anything red, such as a skin rash, is completely absorbed and does not register.

It is recommended that all persons in charge of lecture halls, auditoriums, and so forth make a check of projection conditions. To be fair to the lecturers using the facilities of any meeting place, the correct focal-length projection lens for the distance from the projector to the screen should be employed. The largest possible screen should be used, bearing in mind that considerable tabulated

material will undoubtedly be projected and that it must be readable from the back of the hall.

For deciding on the proper size of screen, a good rule is that the width of the screen should be one sixth of the distance from the screen to the back row of seats. This rule is adequate, and works well when the first row of seats is ten feet or more from the screen. If the screen must be nearer the audience than this, it should be slightly smaller so that the projected image will not appear excessively magnified or distorted.

The projection screen should be chosen with regard to the shape of the auditorium. If most of the seats come within a viewing angle of 25°, as is true in the average lecture hall, a beaded screen will produce the greatest brightness. If the room has small depth but great width, a white screen will produce the best brightness for the majority of the audience. In the latter case vision from an angle of greater than 45° is sure to be distorted.

Pertinent data covering the focal-length of the lens, the distance from the lens to the screen and the size of the image are given in Figure 1. These are based on a 3-inch opening in the slide. Since some slides utilize the entire effective width (3¾ inches), the screen must be large enough to care for these slides also.

Projection screens should be protected from dust when not in use, and the lens mirrors and condensers should be kept spotlessly clean. When projectors equipped with Mazda lamps are used, old, blackened lamps are a prolific cause of poor illumination.

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MULTIPLE EXTRAGENITAL GIANT CHANCRES*

Report of a Case

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RECENTLY a patient with three large ulcerated extragenital chancres was seen at the Massachusetts General Hospital. Two chancres were located on the chin and one in the left inguinal region. A report of this case is submitted not only because of the unusual size of the chancres but also in order to emphasize the importance of considering a diagnosis of primary syphilis in dealing with ulcerated lesions of the skin.

Case Report

A 28-year-old woman first noticed two small papular lesions, one on each side of the chin, on June 10, 1943. One week later, a similar papule developed in the left groin. The three lesions gradually increased in size and became slightly raised and covered with heavy, dark-brown crusts. Two weeks after onset, the right submaxillary lymph nodes became enlarged and so painful that the patient lost much sleep. The lesions themselves were neither painful nor tender.

On July 10, one month after onset, the patient was seen at the Massachusetts General Hospital. The lesions were covered with heavy, oyster shell-like crusts. Each of those on the chin showed, after removal of the crusts, a central ulceration surrounded by a bright-red, slightly raised margin (Fig. 1). The larger lesion, on the right side, measured 3.5 by 4.4 cm., and its central ulceration 1.6 by 2.8 cm. The lesion on the left side measured 1.5 by 1.5 cm., and its central ulceration 0.5 by 0.6 cm. Palpation of the lesions revealed distinct induration of the margins as well as of the bases of the ulcers. Both showed a granulating base covered by a grayish-green membrane of necrotic tissue. The edges of the ulcers were slightly serpiginous and overhanging. There was profuse secretion of a clear, serous exudate in amounts large enough to cause occasional dropping from the lesions. The right submaxillary lymph nodes showed moderate enlargement and considerable tenderness. The left submaxillary, anterior cervical, submental and hyoid lymph nodes were slightly enlarged but not tender.

The lesion in the left inguinal region presented, after removal of the overlying crust, a narrow, cleftlike central ulceration surrounded by a wide area of erosion (Fig. 2). The entire lesion measured 5.5 by 1.5 cm., and the ulcer 1.7 by 0.2 cm. There were the same induration and the same serous secretion as those observed with the lesions of the chin. The left inguinal lymph nodes were moderately enlarged but not tender.

Aside from the three ulcers the skin was normal. There were no lesions on the visible mucous membranes, and on examination by speculum the vaginal mucosa and cervix were found to be free from lesions.

Darkfield examination revealed in each of the three lesions numerous spirochetes whose characteristics conformed to those of *Treponema pallidum*. Aerobic and anaerobic cultures showed only a few colonies of *Staphylococcus albus*. Reactions to both a Hinton and a Wassermann test were positive. Intracutaneous tests for chancroid and lymphopathia venereum were negative.

To avoid a Herxheimer reaction, arsenicals were at first withheld and treatment was inaugurated with five injections of water-soluble bismuth sodium tartrate, 0.2 gm. being given on alternate days. On the day following the first injection, a generalized macular eruption appeared on the skin. A diagnosis of secondary syphilis was made.

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Two days later, scattered brownish-red papules were first noted on the palms and soles.

Ten days after admission, intensive arsenotherapy was begun. For 10 weeks the patient received each week three injections of 0.065 gm. of Mapharsen and one injection of 0.13 gm. of bismuth subsalicylate in oil. The ulcers showed definite evidence of healing 1 week after the first injection of Mapharsen. After 4 weeks of arsenotherapy, two of the lesions — namely, those on the left side of the chin and in

FIGURE 1. *Appearance of the Two Chancres Located on the Chin.*

the inguinal region — had healed. After 7 weeks, the lesion on the right side of the chin had also healed. Surprisingly little scarring remained, and this was limited to the formerly ulcerated areas. There the skin was smooth, atrophic, depigmented and slightly depressed beneath the level of the surrounding skin. On September 16, 8 weeks after the inauguration of arsenotherapy, Hinton and Wassermann reactions were negative for the first time. They have since remained so. An examination of the spinal fluid on July 27, 1943, was negative.

COMMENT

Chancres frequently do not have the appearance of the typical Hunterian chancre. Milian[1] estimates that only 45 to 50 per cent of all chancres are typical in appearance. He names as atypical forms the giant, dwarf, ulcerated, diphtheroid, crusted and hypertrophic chancre.

Extragenital cutaneous chancres often present an unusual appearance. They are as a rule larger and more inflammatory than the genital variety and are often ulcerated and covered by a heavy crust. The inflammation and induration may suggest a furuncle or carbuncle, the crust of an impetigo (ecthyma) or the ulceration of either carcinoma, tuberculosis or tularemia. Stokes[2] has therefore stressed the necessity of a "high index of suspicion" when dealing with ulcers or lesions of the skin that present the diagnostic triad of induration, slow course and satellite adenopathy. Lesions presenting these signs should be regarded as representing a chancre until proved otherwise by repeated darkfield examination of the lesion, as well as of the satellite lymph nodes, and by repeated serologic tests.

In addition to lesions that clinically are only slightly suggestive of chancre but harbor *Trep. pallidum*, there are lesions that strongly suggest a chancre but are nonsyphilitic. Such lesions have been described under the name "pyodermia chancriformis," first by Sánchez Covisa and Bejarano[3,4] and later by Gougerot,[5] Hoffmann,[6] Krantz,[7] Stryker[8] and others. They occur in the genital region, on the extragenital skin and the oral mucosa. It is thus no exaggeration to state that it is impossible to make a definite diagnosis of primary syphilis from the appearance of a lesion alone. In Stokes's words,[9] "the diagnosis of the primary lesion is a laboratory, not a physical or morphologic, problem."

Only with this restriction in mind is it advisable to approach a clinical discussion of the chancre. To the diagnostic triad mentioned by Stokes for extragenital, cutaneous chancres one might add for ulcerated chancres the following two signs: a profuse, purely serous secretion and an eroded border that is usually slightly raised and shows evidence of infiltration. All five signs were present in the lesions

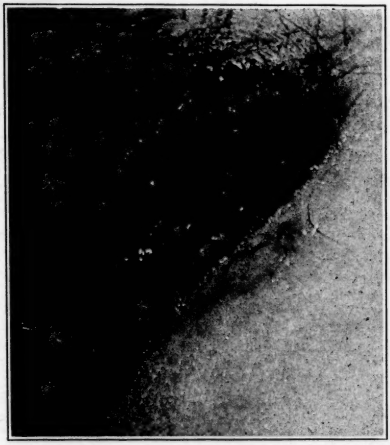

FIGURE 2. *Appearance of the Chancre Located in the Left Inguinal Region.*

of this patient. The presence of an eroded border is believed to be a sign of great diagnostic value. Dreyer[10] has stated that no sign is of such clearness and constancy and so exclusively limited to syphilitic ulcers as is an eroded margin. Its presence is due to the fact that every chancre manifests itself first

as an erosion. If ulceration occurs, it usually affects only the central portion of the erosion and spares the margin.

Ulceration in cutaneous chancres is, according to Fournier,[11] in the vast majority of cases due to necrosis and not to secondary infection. This is the reason why even large ulcerated chancres usually heal with a smooth, superficial scar. The absence of significant bacteriologic findings and the inconspicuous scarring in the case reported here permits the conclusion that the ulceration of the chancres was due to necrosis.

Multiplicity of chancres so far as genital chancres are concerned is not unusual. Most authors have given the incidence as approximately 20 per cent, but some have arrived at considerably higher figures, as, for instance, Driver[12] and Blum,[13] who encountered multiple genital chancres in 38 and 60 per cent of cases, respectively. In extragenital chancres multiplicity is less frequent and probably does not occur in more than 2 per cent of cases. For example, Bulkley[14] observed 1 case of multiple chancres in 116 cases of extragenital chancres, Krefting,[15] 8 in 280, Montgomery,[16] none in 58, Cole,[17] 1 in 61, Tobias,[18] 3 in 65, Downing,[19] none in 38, and Wile and Holman,[20] 1 in 68. In most of the reported cases of multiple extragenital chancres the lesions occurred not on the skin but either in the oral cavity or on modified skin like that of the lips and nipples. Thus, multiple chancres of the extragenital skin can be regarded as uncommon. Still rarer is the presence of chancres at far-distant locations of the skin, as in this case. Queyrat [21] has applied the name "*chancres multipolaires*" to such cases.

Summary

A case presenting three extragenital cutaneous chancres is reported. The chancres were atypical in appearance because of their large size and the presence of deep ulceration.

Many extragenital cutaneous chancres have an atypical appearance. Primary syphilis should therefore be considered as diagnosis for all cutaneous ulcers or lesions presenting the diagnostic triad of induration, slow course and satellite adenopathy, particularly if there is a profuse serous secretion and the margin of the ulcer is eroded.

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MEDICAL PROGRESS

NEUROLOGY*

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PROGRESS in neurology has been greatly influenced by the war. Publication of results of experimental work in the fundamental sciences has been curtailed because of the shortage of physicians, and because much of the research that is being conducted is along lines of vital importance to the war effort and will not be published until after the war. On the other hand, the increase in the incidence of infectious diseases that always accompanies war has given an opportunity to test newer methods of treatment on large numbers of cases, and the global nature of the conflict has awakened new interest in tropical and other diseases that are seldom seen in this country in normal times. In addition, the injuries to the brain and peripheral nerves occurring in war have stimulated investigative work into the mechanism of cerebral concussion and nerve repair. These two topics are omitted from this article since they will be discussed in the review of advances in neurosurgery.

Infectious Diseases

Meningococcal Meningitis

Great strides have been made in recent years in the treatment of meningococcal meningitis. The results obtained with chemotherapy are in striking contrast to those formerly obtained with serotherapy. It is gratifying to note that the use of intraspinal therapy is rapidly being discarded. Uniformly good results in the treatment of meningococcal meningitis by sulfonamide drugs have been reported by various observers. Daniels, Solomon and Jaquette[1] treated 112 patients with meningococcal infections at Fort Bragg, North Carolina, between January 1, 1942, and April 17, 1943. Eighty patients with meningitis and 32 with meningococcemia with no meningitis were treated with sulfadiazine, with only 1 death in the former group and none in the latter. The patients were divided into two groups according to the amount of drug exhibited. The first group received intravenously an initial dose of 0.1 gm. of sodium sulfadiazine per kilogram of body weight, followed by half the initial dose parenterally every eight hours until the patient was able to take the drug by mouth in doses of 1.0 to 2.0 gm. every four hours, so that a blood concentration of 15 mg. per 100 cc. might be maintained. The second group received intravenously an initial dose of 0.05 gm. per kilogram of body weight, followed in four hours by a dose of 0.025 gm. per kilogram. The dose was repeated every eight hours until the patient was able to take the medicine by mouth. The results in both groups were excellent, but the patients who were treated with the smaller doses required a smaller total dosage of the drug than did the others. The duration of fever and length of stay in the hospital were also less in this group, and renal complications were absent, in contrast to the occurrence of hematuria in 15 per cent and anuria in 7 per cent of the group that received the larger dosage.

Hill and Lever[2] treated 68 cases of meningococcal infections with sulfadiazine at Camp Edwards, Massachusetts, between January 1 and April 15, 1943, with no fatalities. They stress the importance of early diagnosis and treatment. Treatment can be instituted without waiting for bacteriologic diagnosis when the four combined symptoms, headache, vomiting, chill and rash, are present. These authors emphasize the necessity of administering the initial doses intravenously and the maintenance of an adequate fluid intake. Thirteen of their patients had meningococcemia with no meningitis. Positive blood cultures were obtained in 40 cases. The spinal fluid was clear in 31 of the 62 cases in which a spinal puncture was done. Organisms were frequently recovered from clear fluids.

Thomas[3] reports an outbreak of meningococcal meningitis and septicemia in the Fourth Service Command between December, 1942, and June, 1943, during which there were 1935 cases. The mortality rate was 3.3 per cent, which is in striking contrast to the 39 per cent mortality reported by Simmons and Michie for the 6000 cases that occurred in the United States Army during World War I. Two thirds of the cases reported by Thomas developed among new troops, and 80 per cent of the 55 fatal cases occurred in this group. Eighteen of the 46 autopsied cases showed hemorrhages into the adrenal glands. This is regarded as an index to the severity of the septicemia and presents an additional feature for therapeutic consideration. Thomas states that early diagnosis and prompt skillful treatment based primarily on administration of suitable sulfonamide compounds will still be important even if prophylactic chemotherapy proves highly effective.

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Ochs and Peters[4] emphasize the importance in the treatment of meningococcal meningitis of following changes in the cerebrospinal fluid by occasional spinal punctures. They treated 39 cases of meningitis and 7 cases of chronic septicemia at Fort Bennington, Georgia, with sulfadiazine or sulfadiazine and serotherapy. There were 2 deaths among the patients with meningitis.

Meyer[5] treated 33 cases of meningococcal meningitis at the station hospital at Camp Grant between January 4 and July 3, 1943, with sulfadiazine, sulfathiazole and polyvalent serum; there were no fatalities. One patient with the clinical picture of the Waterhouse–Friderichsen syndrome recovered.

Smith, Thomas, Dingle and Finland[6] review 51 cases of meningococcal infection among patients admitted to the Boston City Hospital in the two-year period beginning September 1, 1940. There were 43 patients with meningitis and 8 with septicemia without it. There were 9 deaths among the first group and none in the latter. Group II meningococcus, these authors state, should be carefully distinguished from the gonococcus, especially when the organism is recovered only from the blood. They emphasize the importance of intravenous administration of the initial dose of sulfonamide drug, the judicious use of spinal punctures for the relief of symptoms of increased intracranial pressure and the frequency of pulmonary involvement by the meningococcus.

The use of sulfamerazine in the treatment of meningococcal infections is reported by Lepper, Sweet and Dowling,[7] by Gefter, Rose, Domm and Flippin[8] and by Anderson, Oliver and Keefer.[9] Lepper and his associates gave sulfadiazine to 96 patients and sulfamerazine to 22 patients with meningococcal meningitis. The mortality rate in each group was exactly the same, and the duration of the illness and incidence of complications in relation to the virulence of the infection were also the same. Sulfamerazine seems to be as effective as sulfadiazine. In their hands the former drug was slightly more toxic. Gefter and his associates treated 45 cases of meningococcal meningitis with sulfamerazine. The mortality rate was 7 per cent, which is compared with a 58 per cent mortality in 40 cases of this disease at the Philadelphia General Hospital in 1935–1937, and 40 per cent in 50 cases reported in 1942. The results also compare favorably with the mortality rate of 13 per cent in the patients who were treated with sulfadiazine. Toxic reactions to sulfamerazine were noted in 11 per cent of the treated patients. Anderson, Oliver and Keefer found that sulfamerazine was clinically effective in total doses that were on the average half to one third smaller than the amount of sulfadiazine usually administered. Toxic reactions were in general of the same character and occurred with about the same frequency as did those caused by sulfadiazine.

The prophylactic use of sulfadiazine during an outbreak of meningococcal meningitis is reported by Lewis, Bolker and Klein[10] and by Kuhns, Nelson, Feldman and Kuhn.[11] Lewis and his associates cultured the nasopharynx of contacts of patients with meningococcal meningitis. The carrier rate averaged 13 per cent but in some groups was as high as 42 per cent. The carriers were admitted to a special ward and given 2 gm. of sulfadiazine daily for two days and 1 gm. daily for two days. Fluids were forced. No ill effects were noted in 897 carriers. Every person who showed a positive nasopharyngeal culture subsequent to treatment with sulfadiazine was given a course of sulfanilamide. This was necessary in 30 carriers, in all of whom but 1 the culture became negative. The authors state that the use of small doses obviates the risks of toxic reactions to the drug and the need of extensive laboratory facilities. Kuhns and his associates administered 2 gm. of sulfadiazine a day for two days to 15,000 soldiers in residence at two posts where meningococcal meningitis was particularly prevalent during the spring of 1943. Only 2 cases of the disease were reported in the treated cases during a subsequent period of eight weeks' observation, as compared with 40 cases among 18,800 controls. No serious toxic reactions were noted and the treated men continued their usual daily activities.

Fulminating meningococcal septicemia with extensive purpuric hemorrhages into the skin and the adrenal gland has been the subject of numerous reports. Thomas[3] found this combination of symptoms, known as the Waterhouse–Friderichsen syndrome, in 17 of 23 patients who died of septicemia and in 1 additional patient there was edema and congestion of the adrenal glands. Blood transfusion, plasma infusion and adrenocortical extract are recommended by Thomas for the treatment of shock in these patients. In a few cases he obtained good results with epinephrine administered by the constant-drip method. Desoxycorticosterone was used but without clear-cut evidence of benefit. Banks and McCartney[12] submit evidence that the meningococcal adrenal syndrome is a composite entity. It can be differentiated into a pure adrenal syndrome and a mixed or encephalitic one. The former is not necessarily fatal. Eleven cases are reported, 8 of which were fatal. Evidently, prompt diagnosis and immediate treatment of the infection with sulfonamide drugs and vigorous replacement therapy for the adrenal crisis may lead to recovery, at least from the pure adrenal syndrome. Gordon and Shimkin[13] report a case of the Waterhouse–Friderichsen syndrome in which autopsy showed focal necrosis of the pituitary gland, in addition to congestion and microscopic areas of extravasation of red cells into the medulla of the adrenal glands. The authors claim that the changes in the adrenal glands were insufficient to explain the acute adrenal failure, and state that it is possible that the syndrome

resulted from damage to the pituitary gland alone or in combination with the minimal adrenal changes and the effects of the septicemia. Herbut and Manges[14] review the history of the Waterhouse–Friderichsen syndrome and report 4 cases. They conclude that there is no proof that death in these cases is due to adrenal failure rather than to toxicity caused by invasion of the blood stream. Williams[15] reports 17 fatalities resulting from acute fulminating meningococcemia. Adrenal hemorrhages were found at autopsy in only 9 of these cases. He concludes that the adrenal hemorrhage is but an incident in an explosive disease process that overwhelms all bodily resistance.

Bernstein[16] reports a case with causalgia of the right arm and purpuric dry gangrene of the toes and scattered areas of the skin as an example of a rare complication of meningococcal meningitis.

Penicillin Therapy in Bacterial Meningitides

There have as yet been few reports in the literature regarding the value of penicillin in the treatment of infections of the nervous system, and its place in the treatment of meningitis, brain abscess and so forth has not been established.

Pilcher and Meacham[17, 18] report on the use of penicillin in the treatment of meningitis produced experimentally in animals by the intraspinous inoculation of staphylococci and pneumococci. They found that intravenous use of penicillin had no beneficial effect on staphylococcal meningitis. Intrathecal injections, even in small amounts, lowered the mortality rate from 93 to 54 per cent. They resulted in a pleocytosis in the cerebrospinal fluid but no other toxic effects were noted. Similar good results were obtained in the treatment of pneumococcal meningitis. Both intrathecal and intravenous administration of penicillin was necessary in pneumococcal infections, since many of the animals treated only by the intrathecal route died of pneumococcal pneumonia.

Rammelkamp and Keefer[19] studied the concentration of penicillin in the cerebrospinal fluid after intravenous and intrathecal administration in normal subjects and in patients with meningitis. Penicillin did not pass through the blood-brain barrier in significant quantities when injected intravenously. After the intrathecal injection of 5000–10,000 Florey units, penicillin was slowly absorbed and slowly excreted in the urine. It was detected in the cerebrospinal fluid thirty-one hours after injection of 10,000 units. Absorption from the subarachnoid space was more rapid in the patients with meningitis. It was found at autopsy in the fluid from both the cisterna magna and third ventricle of 2 patients who had received the agent intraspinously several hours before death. In normal subjects the intraspinal injection of 10,000 units caused headache, vomiting, increased intracranial pressure and pleocytosis in the cerebrospinal fluid similar to that seen after the intraspinal injection of serum, lipiodol or air. The intraspinal injection of 5000 units in normal subjects produced only slight headache and slight pleocytosis in the cerebrospinal fluid. The intrathecal injection of 3000 to 10,000 units in patients with meningitis produced no untoward symptoms. Since penicillin is known to be extremely effective as an antibacterial agent against the streptococcus, pneumococcus and staphylococcus and since meningitis and brain abscess caused by the latter two are resistant to sulfonamide therapy, Rammelkamp and Keefer suggest that the intrathecal injection of penicillin may be a useful method of treating these conditions. Since an effective concentration of the active substance can be maintained for about twenty-four hours without undue toxic reactions, the initial dose should not exceed 10,000 units and subsequent injections of 5000 units may be given every twenty to twenty-four hours. If bacteremia is present, penicillin should be given intravenously as well as intraspinously.

Evans[20] used penicillin in the treatment of 1 patient with pneumococcal meningitis and 2 patients with staphylococcal meningitis, with recovery in all 3 cases. In the first case, pneumococcal meningitis developed following fracture of the skull. In the second case, infection of the meninges by the staphylococcus was secondary to sinusitis and intracerebral abscess. The third patient developed staphylococcal meningitis subsequent to an operation for the removal of a cord tumor in the cervical region. Large doses of penicillin were administered intravenously, intramuscularly and intrathecally in all 3 cases. Sulfadiazine was also used in the treatment of the first patient, but Evans gives the major credit for the cure to penicillin and thinks that its intrathecal administration of penicillin in such cases is of great value.

Cerebral Malaria

Infection with malaria organisms is one of the major problems of military medicine, and as a result the literature of the past year contains numerous articles on various aspects of the infections, including the symptoms and signs of cerebral involvement.

Simpson and Sagebiel[21] report 12 cases of cerebral malaria that were treated at a United States naval base hospital without a fatality. The dominant symptom was sudden onset of convulsions and coma. An acute confusional psychosis developed in 6 cases. The febrile reactions were highly irregular, with no tendency to follow a forty-eight-hour cycle. The cerebrospinal fluid was examined in 8 cases. It was under increased pressure, and pleocytosis was present in those cases manifesting marked meningeal symptoms. They state that prognosis depends on early diagnosis and prompt treatment. Quinine dihydrochloride, 7½ gr. in 250 cc. of normal saline solution, was administered

intravenously every eight hours until the patients were able to take quinine by mouth. Sedation and absolute bed rest are considered of importance in the therapy.

Talbot[22] calls attention to the fact that malaria may stimulate disease of every part of the body, and that the absence of chills and fever should not rule out its occurrence in people who are living or have lived some time in the past in the tropics or other areas of endemic malaria. He divides the atypical cases into twelve groups, four of which are of special interest to the neuropsychiatrist. In one group there are various manifestations of cerebral malaria, with headache, fever and prostration simulating medical shock, heat exhaustion, acute alcoholism, acute mania or an afebrile psychosis. The symptoms clear up or greatly improve on antimalarial therapy. In the second group there is complaint of visual disorder, with headache, often of long duration. Some of the patients have typical optic neuritis, with clouding or dimness of vision, temporal or frontal headache and deep pain in the orbit, which is made worse by ocular pressure. Under antimalarial therapy these patients improve, some with varying degrees of residual visual impairment. Patients in the third group have signs and symptoms of other cranial-nerve involvement, frequently that of the eighth nerve, with resulting vertigo and deafness. A pure malarial basilar meningitis is sometimes seen. The fourth group comprises patients with vague complaints of neuralgia, fatigue or other inconsequential symptoms often labeled as psychoneurotic. The diagnosis of malaria is established by the findings of positive blood smears, and the symptoms are relieved by quinine therapy.

Most and Meleney[23] stress the importance of early diagnosis and adequate treatment of infections with *Plasmodium falciparum*. Unless one is familiar with the extremely varied clinical picture that infection from the organism may assume and the possibility of the development of alarming symptoms requiring early and intensive therapy, the infection may remain unrecognized and may even terminate fatally. Stupor and coma are the most frequent evidences of involvement of the nervous system. In some cases convulsions, stiffness of the neck, hyper-reflexia and the Babinski sign are present. Occasionally there is intermittent rigidity or sucking and grasping reflexes. Incontinence of the sphincters is frequent. On the whole, the clinical picture is similar to that seen in acute meningitis or encephalitis. Mental symptoms are occasionally the outstanding feature at the onset and may result in the admission of the patient to a psychiatric institution. Confusion, restlessness and negativism are usual findings. Such patients must be watched closely, since they may become manic or commit suicide. Quinine dihydrochloride, 0.6 gm., should be given intravenously every four hours to patients in coma or with predominant cerebral signs. Spinal drainage may be of value in restoring consciousness. Fluids by vein should be administered freely, and nicotinic acid in doses of 100 mg. should be added to the infusion along with each dose of the quinine dihydrochloride in order to secure maximal dilatation of the cerebral capillaries.

The pathology of cerebral malaria is described by Dhayagude and Purandare.[24] In the course of fifteen years they found malarial parasites in the capillaries of the brain in 55 of 97 cases of malaria. Fever and coma were present in 28. Other symptoms included paresis of the limbs, aphasia, dysentery, pneumonia, rigidity of the neck and exaggerated reflexes. The brain appeared grossly normal in 12 of the 55 cases, and in the remaining 43 there was a slate-gray discoloration of the brain substance. On microscopic examination the capillaries of all 55 patients were filled with malarial parasites and their pigment. Punctiform hemorrhages were found in the subcortical region in 2 cases. Malarial granuloma was present in 10 cases. Older granulomas consist of a central capillary surrounded by a mass of neuroglial cells. *P. falciparum* was the infecting type of parasite in the cases with granuloma. The granulomatous lesions, according to these authors, provide the pathological basis for mental disturbances designated as "malarial psychosis."

Subdural Empyema

Kubik and Adams[25] present a study of 14 patients with subdural empyema. Their article is the most complete analysis of the clinical features and pathological observations yet recorded in the literature. The sources of infection were paranasal sinusitis in 12 cases, otitis media in 1 case and bronchiectasis with metastatic infection in 1 case. The symptoms in the cases complicating sinusitis were fairly uniform and consisted of exacerbation of chronic sinusitis, orbital swelling, headache, at first localized and later becoming generalized, fever, stiffness of the neck, drowsiness or stupor and focal neurologic signs. Hemiplegia or hemiparesis was present in nearly all cases, and Jacksonian seizures often occurred. The cerebrospinal fluid was under increased pressure, with an increase in cell count and protein content. The sugar content was normal, and the fluids were sterile. The course was rapidly progressive, death in 12 cases occurring within six to twenty days after the onset of the headaches. Two patients recovered after surgical drainage of the empyema. Infection of the subdural space occurred by direct extension through the dura or as a result of thrombophlebitis of the venous sinuses. The subdural pus covered the greater part of the lateral surfaces of the frontal lobe, and in the corresponding area there was a localized subarachnoid exudate but scarcely any generalized leptomenin-

gitis. In the underlying cortical gray matter there was severe ischemic necrosis and in most cases thrombosis or thrombophlebitis of the subarachnoid veins. Surgical treatment should consist of drainage through a craniotomy and not through the frontal sinus or a mastoidectomy wound.

Mumps

McGuinness and Gall[26] analyze the data on 1378 cases of mumps at Camp McCoy, Wisconsin. Neurologic complications were present in 55 cases (4 per cent). Headache, nausea, drowsiness and stiff neck were the symptoms and signs indicative of involvement of the nervous system in all but 3 of these 55 patients. In these 3 the syndrome was that of a primary subarachnoid hemorrhage in one patient, that of an intracerebral hemorrhage in the second and that of an acute polyneuritis with facial diplegia in the third. The cerebrospinal fluid was bloody in the first two cases, and in the third the fluid contained 16 white cells per cubic millimeter and 135 mg. of protein per 100 cc. The first patient had a mild parotitis, and in the third patient the signs of involvement of the nervous system developed twenty days after the onset of parotitis. In the second case there was no parotitis and the diagnosis of mumps was based on a complement-fixation test. The authors attribute the neurologic involvement in all 3 cases to the mumps infection but it seems more likely that they were only coincidental complications.

Herpes Zoster

Denny-Brown, Adams and Fitzgerald[27] report on the pathologic features of 3 cases of herpes zoster. In 2 patients the herpetic eruption was in the thoracic region and the corresponding dorsal root ganglion was the site of an inflammatory necrosis. In addition, there were degeneration of the related motor and sensory roots, severe neuritis, unilateral segmental poliomyelitis and localized leptomeningitis. The third case, with eruption in the occipital and auricular regions and a transient facial (Ramsay–Hunt syndrome) and lingual palsy, was of special interest because of the rarity of autopsy examination in such cases. The authors found necrotizing ganglionitis of the second cervical ganglion, unilateral segmental poliomyelitis in the cervical cord, motor neuritis of the facial nerve and mild inflammatory reaction in the medulla. There was no destruction of the cells in the geniculate ganglion, but some lymphocytic infiltration was present in the fibers of the facial nerve adjacent to the ganglion.

Taterka and O'Sullivan[28] report 2 cases of herpes zoster with paralysis and atrophy of muscles of the extremities and summarize the data on 42 previously reported cases. The muscular involvement does not necessarily coincide with the herpetic eruption in localization and extension. The time interval between the vesicular eruption and appearance of paralysis may range from one day to two months.

Poliomyelitis

The concepts of muscular dysfunction in anterior poliomyelitis advanced by Sister Kenny were subjected to analysis by Watkins, Brazier and Schwab[29] and Moldaver.[30] Watkins and his associates, who used the electromyograph, state that of the three concepts of Kenny the only one upheld by objective measurement is that of inco-ordination and that this term is misleading. They demonstrated not only simultaneous activation of protagonist and antagonists but also intermittent synchrony of single discharges from opposing muscles such as is found in peripheral-nerve injuries during regeneration of axones. "Disordered reciprocal innervation" seems to be a more descriptive term for this type of dysfunction. Moldaver[30] explored neuromuscular degeneration in poliomyelitis by the chronaxie method; the so-called "spasm" was studied in some patients, mostly by electromyograms. He concluded that "spasm" does not lead to neuromuscular degeneration. In paralytic and paretic muscles, called "alienated," there is always some degree of neuromuscular degeneration. Among these muscles some are partially denervated; these have a good chance to recover. Others are totally denervated and cannot therefore recover. There is no clinical evidence of so-called "inco-ordination" in the ordinary sense. The patient attempts voluntarily or involuntarily to use a stronger muscle for a weak or paralyzed one. This abnormal use of an extremity is substitution and not inco-ordination.

Rickettsial Diseases

Dyer[31] reviews the rickettsial diseases and points out the constancy of cerebral symptoms in epidemic and endemic typhus fever. Nervous and mental symptoms are also frequent. In Rocky Mountain spotted fever there are restlessness, insomnia, disorientation and, in severe cases, delirium. In fatal cases coma usually precedes death.

Epilepsy

Diagnosis

In civil life the diagnosis of epilepsy can be established by observation of the patient over a period of months or years. In military hospitals it is important for various reasons to establish the diagnosis as soon as possible. In patients with infrequent seizures, the main diagnostic aids are electroencephalography and the observation of seizures artificially produced by hydration or overventilation.

Garland, Dick and Whitty[32] used the water-Pitressin test in 96 patients, including 20 controls. The patients were kept in bed throughout the test and for twenty-four hours afterward. Five hundred

cubic centimeters of water was given hourly from 7 a.m. until the test was discontinued, the usual total being 5500 cc. Pitressin was given hourly from 10 a.m. onward, the doses being 0.2, 0.3, 0.4 and 0.5 cc., followed by four doses of 0.5 cc. each. Blood-pressure readings were made at frequent intervals, and the patient was weighed every three hours. Fluid intake and output, including vomitus, were also measured to determine the amount of fluid retention. If a fit occurred, the test was stopped at once and 1 gr. of phenobarbital was given by mouth. It was also stopped if there was severe and distressing vomiting, abdominal discomfort or severe and persistent headache. Fits usually occurred from 5 p.m. onward. No serious untoward effects were noted. Convulsions resulted in 17 (39 per cent) of the 44 patients with epilepsy, 12 (38 per cent) of the 32 patients with doubtful epilepsy and in none of the 20 control patients with hysterical personalities.

Schwab[33] found the electroencephalogram to be of great value in the diagnosis of epilepsy in a Navy hospital.

Robinson[34] tested the value of hyperventilation and the electroencephalogram in the diagnosis of epilepsy. One hundred and forty-six patients were subjected to a six-minute period of hyperventilation. Seizures occurred in 14 (10 per cent). The seizures were of the petit-mal type in 12 patients and of the grand-mal type in 1, and took the form of involuntary crying in 1. The seizures that resulted from hyperventilation were similar to the patient's spontaneous seizures. The petit-mal seizures occurred during hyperventilation. The single grand-mal seizure followed the period of overbreathing by two and a half minutes. Of the 14 patients who had a seizure related to hyperventilation, the resting electroencephalogram was abnormal in 12 (85 per cent). The electroencephalogram showed slow waves on hyperventilation during seizures in all 14 cases. Robinson concludes that the value of overbreathing in the diagnosis of epilepsy lies in its simplicity of application and the specificity of response that is induced. It enables the physician to observe the actual seizure pattern. The disadvantages are that seizures result in only a small percentage of cases and that the method requires the active co-operation of the patient. The test does not exclude bizarre hysterical episodes. By contrast the electroencephalogram has the advantages of permanency of record, the need of a minimum degree of co-operation on the part of the subject, the possibility of localizing the focus of a circumscribed lesion and wave forms that are often specifically diagnostic in themselves. The disadvantage is the nonspecificity of the abnormal potentials occurring in some of the relatives of epileptics, in some persons with mental deficiency, psychosis or behavior disorders and in cases of increased intracranial pressure.

Merritt and Brenner[35] report on 3 patients with convulsive seizures who had normal air encephalograms, seven, twenty and thirty months, respectively, after their first convulsions but were subsequently proved to have brain tumors. Cerebral tumors, they say, are not apt to produce any change in the ventricular system unless they are large enough to produce focal neurologic signs or increased intracranial pressure. If in the absence of these it is decided that an air study is advisable, a negative report should not be accepted as conclusive proof that no tumor is present.

Treatment

Cohen, Coombs, Cobb and Talbott[36] found that azosulfamide exhibited anticonvulsive action in patients with epilepsy. Associated with the anticonvulsive effects were a decrease in the carbon dioxide power of the serum and an elevation in serum chlorides. In comparing the changes in the serum produced by azosulfamide with those accompanying the administration of phenobarbital they found that a positive potassium balance coincided with the anticonvulsive effect of both drugs. Ammonium chloride produces the same degree of acidosis as does azosulfamide, without alteration of potassium exchange, but the former has no anticonvulsive effect. Phenobarbital produces no acidosis but a positive potassium balance and has an anticonvulsive effect, which suggests that the acidosis is not necessarily the crucial factor in anticonvulsant action.

Davidoff and Doolittle[37] used sodium 5-ethyl, 5-(methyl, 1-butenyl) barbiturate (Delvinal Sodium Vinobarbital) in the treatment of patients with convulsive seizures. They found that it was more effective than phenobarbital in the control of petit-mal seizures and did not produce the degree of drowsiness that follows the administration of the latter. Because of its effect on psychomotor activity it is a valuable adjunct to other anticonvulsant drugs, such as Dilantin Sodium, in the treatment of grand-mal or severe motor seizures. Because of its rapid action and relatively low toxicity, the oral administration of the drug is of distinct value in the treatment of serial seizures and their sequelae.

Price, Waelsch and Putnam[38] report that *dl*-glutamic acid hydrochloride is beneficial in the treatment of petit-mal and psychomotor seizures. Petit-mal seizures were decreased in frequency, and there was subjective and objective improvement in the mental and physical alertness of the patients. Grand-mal seizures were not affected by administration of the drug.

Intracranial Aneurysms

Intracranial aneurysms continue to receive considerable attention. Sahs and Keil[39] review the clinical features in 64 cases in which the diagnosis

of subarachnoid hemorrhage caused by ruptured intracranial aneurysm was made. The presence of aneurysm was verified at autopsy in 12 cases. Eighteen of the 64 patients died in the hospital, 22 were discharged well, and 24 were improved but were left with sequelae such as hemiplegia, ocular palsy, aphasia and disturbance of the visual fields.

From a study of 10 cases, Globus and Globus[40] conclude that rupture of an intracranial aneurysm into the substance of the brain and into the ventricles is preceded by softening of brain surrounding the vessel. Changes in the brain tissue parallel the progressive pathologic alterations in the aneurysmal wall that culminate in its rupture. The escaping blood breaks through a residual zone of partially softened brain tissue separating the so-called "hemorrhagic cavity" from the adjoining compartment of ventricular cavities, and floods the latter as the fatal termination. A fatal issue occurred as the result of intracerebral and intraventricular hemorrhage in 10 of the 20 verified cases of intracranial aneurysm.

Polycythemia Vera

Tinney, Hall and Giffin[41] report neurologic symptoms in 78 per cent of 163 cases of polycythemia vera. Fifty-five patients sought treatment primarily because of neurologic complaints. Subjective complaints, such as weakness, fatigue, insomnia, drowsiness, irritability and loss of memory, were so frequent, nonspecific and varied that patients exhibiting them were thought to have a functional disorder. Objective neurologic signs occurred in 17 per cent of the series and resulted from thrombosis of a cerebral vessel or from cerebral hemorrhage.

Periodic Paralysis

Brown, Currens and Marchand[42] describe a hitherto unrecognized syndrome associated with potassium loss in patients with chronic nephritis. The syndrome is characterized by episodes of flaccid paralysis of the extremities resembling that seen in familial periodic paralysis, low T waves in the electrocardiogram similar to those seen in patients with potassium depletion, and signs of chronic nephritis. The authors conclude that the muscular weakness and the electrocardiographic changes are related to the low level of potassium in the serum, which results from the excessive excretion of potassium by the diseased kidneys.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 30321

PRESENTATION OF CASE

First admission. A forty-four-year-old musician entered the hospital because of weakness and tarry stools.

The patient had been in apparent good health until thirteen years before admission, when he developed epigastric pain coming on a few minutes to two hours after meals. It was not severe, was aggravated by excitement and was relieved by soda at first and by Amphogel later. It radiated through to the back. The attacks would last for a few weeks and then disappear for months. Eight years before entry he had an episode of feeling faint and noticed profuse perspiration, followed by the passage of a dark molasses-like stool. He fainted and was taken to a hospital in another city. He was given several blood transfusions and was discharged. Since that time he had had recurrent attacks of similar character, for which he was admitted to a community hospital nine or ten times. Repeated and extensive studies in that hospital were negative except for blood in the stools and a mild hypochromic anemia, for which he was repeatedly transfused. A gastroscopy was said to show a gastric polyp and possibly a benign peptic ulcer.

Since the first episode the patient had more or less limited himself to a bland diet and had taken six meals daily. Although he led a rather strenuous and perhaps irregular life, he did not drink alcoholic beverages or smoke. Asparagus, turnips and cabbage gave him hives. Fried foods brought about epigastric pain. No statement was made about the relation of the pain and the bleeding. He had had no jaundice or clay-colored stools. He had had no sore tongue, difficulty in swallowing or genitourinary or cardiorespiratory symptoms.

The patient had lived in the Philippines until he was nineteen years old. He had had smallpox as a child but had had no other known illnesses.

Physical examination showed a well-developed, well-nourished pale man in no distress. The heart and lungs were normal. There was moderate mid-epigastric tenderness to deep palpation, but no masses or spasm.

*On leave of absence.

The blood pressure was 120 systolic, 80 diastolic. The pulse was 82, the temperature 99°F., and the respirations 20.

Examination of the blood showed a red-cell count of 5,300,000, with 12 gm. of hemoglobin, and a white-cell count of 7600, with 75 per cent polymorphonuclears, 20 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils. The platelets were normal. A blood Hinton test was negative. The urine was normal. Two guaiac tests on stools were negative. The blood serum nonprotein nitrogen was 24 mg. per 100 cc., and the protein 9 gm. The prothrombin time was normal, and the clotting time 7 minutes. The hematocrit was 46.8 per cent. The corrected sedimentation rate was 1.7 mm. per minute. A second hematocrit was 42 per cent. A bromsulfalein test gave 5 per cent retention. A tuberculin test with a 1:50,000 dilution was negative.

A gastrointestinal series showed a normal esophagus. The stomach contained a small amount of fluid. No definite polyp or ulcer crater could be demonstrated. The duodenal cap was quite tender and on a spot film showed an area suggestive of a small crater on the posterior wall. Fluoroscopic examination of the chest showed areas of increased density in the right upper lobe and shadows that were suggestive of small cavities.

Following the x-ray films of the chest two gastric aspirations were examined for acid-fast bacilli, without success. Sputum examinations were also negative. For a while the patient was put under respiratory precautions. At the end of the second hospital week a gastroscopy revealed a network of what appeared to be dilated veins 1 to 3 mm. in diameter covered with a rather smooth slightly reddened mucosa; they were situated on the anterior wall, extending from the angulus to the cardia. Examination was otherwise negative. A repeat gastrointestinal series showed no additional findings. The patient was discharged against advice on the fifteenth hospital day.

Second admission (five months later). Following discharge the patient was in excellent health for three weeks, having had no recurrence of epigastric pain or of tarry stools. At that time, following an upper respiratory infection, he passed a black stool and was admitted to a community hospital for ten days. There was no further melena and he was sent to this hospital for further studies.

Physical examination was essentially the same as before.

The blood showed a red-cell count of 3,160,000, with 7 gm. of hemoglobin, and a white-cell count of 4200, with 56 per cent polymorphonuclears, 40 per cent lymphocytes and 4 per cent monocytes. The red cells were hypochromic, with moderate variation in the size of the cells. The urine was normal. One stool examination showed a ++ guaiac test. The nonprotein nitrogen was 28.5 mg. per 100 cc., and the protein 8.4 gm., with 6.1 gm. of albumin

and 2.3 gm. of globulin. The cephalin-flocculation test was ± in twenty-four hours and ++ in forty-eight hours. A bromsulfalein test showed 5 per cent retention.

A gastrointestinal series revealed considerable thickening of the mucosal folds in the stomach, without definite ulceration. The distal part of the duodenum remained narrow, and there was slight irregularity in the area previously described that was suggestive of a crater. The remainder of the examination was negative. X-ray films of the chest revealed no change from the previous examination. Gastric aspiration showed no acidity in the original contents or in that twenty-four hours after histamine; there was a + guaiac test.

A gastroscopy showed essentially the same findings as noted before, with the addition of two areas on the anterior wall that measured 4 mm. in diameter and were white. There was no blood in the stomach.

The patient was given several transfusions of whole blood, and on the twenty-first hospital day an operation was performed.

Differential Diagnosis

Dr. E. Stanley Emery, Jr.* This protocol presents a forty-four-year-old musician who, for thirteen years, had suffered from epigastric distress, which could have been compatible with a duodenal ulcer. For eight years he had been having frequent attacks of gastrointestinal bleeding. Another possibly important point in the history is that he lived in the Philippines until he was nineteen years of age. He is said to have been allergic to certain foods and had what appears to have been a chronic stationary process in the right upper lobe of his lung. X-ray study revealed a narrowing and slight irregularity of the duodenum that was suggestive of a crater, but I gather that it was not considered characteristic for a duodenal ulcer. Furthermore, gastroscopy revealed a curious network of what appear to be dilated veins on the anterior wall of the stomach. The protocol suggests that bleeding was the major problem. From the data presented we have to decide why this patient continued to bleed.

The leading questions are as follows: Did this patient have an ulcer? Was ulcer alone responsible for the bleeding or was there another condition superimposed or co-existent with an ulcer? Was there some condition that was not only responsible for the bleeding but also simulated an ulcer?

Bockus[1] lists twenty-three causes for gastrointestinal bleeding, and it is obvious that in the time allotted I cannot discuss all these causes. I am therefore going to consider the findings as presented with the hope that I may get a clearer idea of the nature of the symptoms and the laboratory findings and then discuss those things that seem most pertinent.

The protocol tells us that the patient had been in good health until the age of thirty-one, when he developed epigastric pain that was not severe. I wish that I knew more about the nature of the symptoms because a differential diagnosis involving the question of ulcer may be settled by an accurate evaluation of the symptoms. It might be helpful to know whether the distress coming on a few minutes after eating was the same or different from that beginning two hours after eating. The exact point to which the distress radiated to the back might also have some diagnostic significance.

Eight years before entry he had the first of a number of severe bleeding attacks for which he was studied nine or ten times at a community hospital. All these studies were apparently negative except for a mild hypochromic anemia and a gastroscopy that was said to have shown a gastric polyp and a suggestion of a benign peptic ulcer. It would be helpful to know who did the gastroscopy, since the value of procedures of this kind is in direct proportion to the experience and ability of the man performing them. The polypoid appearance may be of significance and will be discussed further later on.

The patient had followed a somewhat limited diet, consisting of six meals daily, but we are not told whether the painful symptoms were ameliorated by the frequent feedings. He did not drink alcohol, which eliminates one cause of portal cirrhosis. He was allergic to asparagus, turnips and cabbage, in that they gave him hives. Fried foods brought on epigastric pain, but we are not told whether this was the same type of pain of which he usually complained. I should like to know this, although I gather little significance was given to this fact, since there is no statement that x-ray films of the gall bladder were taken. I cannot lay much importance to this statement because many patients, either with or without organic disease, complain of indigestion from fried foods that has to do with the way they are cooked or something of that sort. It is said that no statement was made about the relation of pain and bleeding. I am not sure why this was put in; furthermore, if there were a positive relation, I should not know how to interpret it. The patient had never had clay-colored stools, which is negative evidence for biliary disease. He had had no sore tongue or difficulty in swallowing; in other words, no evidence was found for a deficiency. There were no genitourinary or cardiorespiratory symptoms. The history therefore does not suggest that the bleeding was secondary to cardiac insufficiency.

Having lived in the Philippines until he was nineteen years of age causes us to think of some parasitic infestation as the cause of the gastrointestinal bleeding. I have seen one patient infested with *Ascaris lumbricoides* who had definite attacks of epigastric

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pain simulating an ulcer that were completely relieved after expulsion of the worms. Hookworm infestation may cause bleeding, usually of a chronic type. Schistomiasis is another disease that is a frequent cause of bleeding, but the mechanism is a liver cirrhosis, for which there is no evidence in this case. Furthermore, I assume that the patient was carefully studied for parasites in the stools and no mention of their presence is recorded. There was no eosinophilia and, therefore, I think that this possibility can be ignored.

The protein was 9 gm. per 100 cc., and at a later admission, 8.4 gm. with 6.1 gm. of albumin and 2.3 gm. of globulin. This marked elevation of blood protein is difficult to understand, and in talking with Dr. Howard Armstrong he could make only two suggestions: either it was the result of marked dehydration or the test was done in an extremely hot laboratory. The first hematocrit was 46.8 per cent, and the second 42 per cent, neither of which suggests marked dehydration. There is nothing in the history to suggest dehydration, although the red-cell count was high for a person who had been recently bleeding. The sedimentation rate was very rapid, which may be evidence for something more than a peptic ulcer. A gastrointestinal series showed a tender duodenal cap and an area suggestive of a small crater on the posterior wall. At the time of the first report no mention was made that the duodenum was narrow, but a second report stated that it remained narrow. I wonder if I may see the x-ray films.

Dr. Laurence L. Robbins: These films were picked out at random, and they demonstrate the process in the right upper lobe. The lesion has the appearance of a rather long-standing tuberculous affair.

Dr. Emery: One wonders whether these findings could have been due to some fungus infection, which, although rare, can produce lesions in the gastrointestinal tract that are responsible for pain and bleeding. Actinomycosis and blastomycosis have both been reported in the duodenum, but they are extremely rare. A second examination of the lungs five months later reported no change, which I suppose argues against a fungus or any active process in the chest, but I should like to get the opinion of the roentgenologist on this point.

Dr. Robbins: It certainly could be a fungus infection.

Dr. Emery: Would the fact that it had not changed in five months tend to rule it out?

Dr. Robbins: No; furthermore, tuberculosis may show no change by x-ray over a long period of time.

The gastrointestinal examinations were done at various times. We can definitely rule out varices of the esophagus. The area that was questioned several times about the possibility of a crater was this narrow distal portion of the cap, but we could never be positive about it. These are thickened mucosal folds in the cap and make one suspicious of some inflammatory process in that area. The stomach shows some thickening of the mucosal folds and some increase in the amount of secretion, both of which are consistent with gastritis.

Dr. Emery: Are these the dilated veins?

Dr. Robbins: I doubt if one can recognize a dilated vein 3 mm. in diameter. At the last examination the distal portion of the cap remained narrow.

Dr. Emery: It was not very constricted.

Dr. Robbins: As you see it is fairly narrow and does not open up to normal width. I see nothing that suggests polyp in the stomach.

Dr. Emery: Am I right in believing that these findings are not characteristic of duodenal ulcer?

Dr. Robbins: Certainly there is no positive evidence of a crater. It is only suggestive of one.

Dr. Emery: At the end of the second week in the hospital a gastroscopy revealed what, to me at least, is an unusual condition, namely, a network of dilated veins, 1 to 3 mm. in diameter; they were covered with a rather smooth, slightly reddened mucosa and were situated on the anterior wall, extending from the angulus to the cardia. This is an unusual finding and I am not entirely clear from this description just what the condition suggested. If Dr. Edward B. Benedict is here I hope that he will tell us a little more about it. Offhand, it makes one think of an increase in portal pressure, but so far we have nothing else to go with such a condition. It is not my idea of a spider angioma, which, of course, is a cause of frequent and severe bleeding in the gastrointestinal tract. Usually one makes the diagnosis of this condition by finding evidence for it in either the pharynx or larynx, but no mention of any such finding is made.

Schindler[2] reports having seen dilated veins in only one case and that patient had a carcinoma of the pancreas that was compressing the portal system. He did not state whether esophageal varices were also present. I do not know whether such a condition can be caused by an allergy, although it seems unlikely.

Dr. J. H. Means: The abstract gives a false impression of Dr. Benedict's findings. I saw this man on the last admission and struggled a great deal, diagnostically speaking. At the first gastroscopic investigation Dr. Benedict found what he believed to be gastric varices but no evidence of esophageal varices. The second gastroscopic examination was different. The findings were consistent with gastric atrophy, and he doubted that the patient had real gastric varices.

The reason the patient spent nineteen years in the Philippines is that he was a Philippino.

Dr. Emery: The patient was discharged against advice but readmitted five months later, having continued to bleed off and on in the interim. The essential findings on the second admission were an

anemia of 3,100,000, a hemoglobin of 7 gm. and a white blood-cell count compatible with this anemia. The serum protein was again elevated, as already mentioned. In addition, a cephalin-flocculation test was ± in twenty-four hours and ++ in forty-eight hours, which, to my way of thinking is essentially negative. After several transfusions the patient was explored on the twenty-first hospital day.

In trying to evaluate this case the first question to settle is whether this man had a duodenal ulcer. This we shall have to decide on the basis of the pain radiating through to the back and the intermittency of the distress. It could have been duodenal ulcer, but it was certainly not characteristic of duodenal ulcer. Gastroscopy suggested trouble in the anterior wall of the stomach and, at one time, dilated veins. A later gastroscopy gave the impression of atrophy of the mucous membrane. One thing against ulcer is the somewhat atypical x-ray picture after thirteen years of the trouble. If ulcer was present, could it have explained the peculiar nature of the veins in the stomach? Ulcers, of course, can be responsible for large amounts of bleeding. The general history, the fact that this patient was allowed to go for so long a time without surgery and the fact that the case is being presented for a clinicopathological conference all suggest, however, that something else was responsible for the bleeding.

It is hard for me to believe that this man had a fungus infection for fourteen years. So I shall have to rule it out on that basis. How about tuberculosis? If this was tuberculosis of the lung, and I understand that the x-ray findings were compatible with it, a tuberculous infection could have developed in that portion of the gastrointestinal tract and could have produced chronic lesions that might perhaps bleed from time to time. Against it, however, are the location and the fact that it would be extremely uncommon for tuberculosis to produce as much bleeding as this man had. Although we see tuberculosis around the duodenum at times, the commonest place is in the ileocecal region.

Could the bleeding have been the result of a food allergy? In view of one case that I have observed, it would seem as though it could. This patient was a man of twenty-five who had always suffered from hives on eating certain foods. For some time before we saw him, he had suffered from hunger pains. He entered a hospital because of a recent attack of severe bleeding, which lowered his red-cell count to 2,500,000. Further observations on the part of the physicians and the patient revealed that three conditions were necessary to produce the bleeding: that he eat onions, that he eat a heavy meal with them, and that he be nervously tired. Any one of these conditions alone did not seem to bring on an attack, but the combination of all three inevitably did.

Could allergy explain the gastroscopic appearance in this case? There is little in the literature that I have been able to find along these lines. Schindler[2] quotes others but does not give any opinion of his own. Almost all gastroscopic observations in allergic individuals confirm the existence of a simple gastritis. The patient of whom I was just speaking had four gastroscopic studies. Three were done in England. The first examiner reported a normal stomach; the second, numerous erosions with bleeding; the third, a large wheal where the instrument touched the mucosa, which bled profusely within fifteen seconds. The fourth examination was made at a large medical clinic, where the mucosa was reported as pale and flaccid, suggesting a catarrhal type of gastritis. At times, a portion of the mucous membrane became edematous, resembling closely the mucous membrane of a nasal polyp. One wonders whether the first gastroscopic examination in this patient, which was said to have shown a gastric polyp, may have been a similar type of finding. It is difficult, however, to explain the dilated veins on the basis of allergy. Could these dilated veins have been the result of increased portal pressure? There is no evidence for liver disease or increased portal pressure other than those veins. Dr. S. Burt Wolbach told me that he had seen portal stasis as a result of pressure from enlarged lymph nodes, and another physician told me that he had seen a case in which a duodenal ulcer had caused thrombosis of the portal artery, with recanalization. As previously stated, Schindler[2] reports only one case of dilated veins in the stomach, which was the result of a pancreatic carcinoma interfering with the portal circulation.

I do not have the slightest idea what this man had, but in order to make a diagnosis I shall guess that he had a duodenal ulcer, acute allergy and perhaps portal involvement causing pressure on the veins. It is possible, in view of the experience with the patient just mentioned, that the bleeding was not the result of any one of these things, but was caused by a combination of all.

DR. MEANS: I might tell Dr. Emery that, so far as I know, no one made the correct diagnosis on this man until he was explored — neither the physicians nor the surgeons. When I first saw him, at the time of the last entry, I thought he probably had an occlusion in the splenic vein. I was much impressed with Dr. Benedict's gastroscopic report and disappointed when he back-watered on the second, so to speak. There are other points that we did not emphasize so much as Dr. Emery has, perhaps we should have. The striking thing was the bleeding. The surgical consultant thought that the man had a duodenal ulcer. I thought that he did not have an ulcer but I did not know what he had, unless it was splenic-vein occlusion. We could find no evidence of tropical disease. He had been in this country a great many years.

DR. ALLAN M. BUTLER: I have just been looking through the record to check the serum protein values. There is little doubt that they were high. The values varied on repeated analysis from 9.0

to 7.6 gm. per 100 cc. The albumin-globulin ratios, as is often the case, were not too constant. Errors can be readily made in that determination. In one instance the protein was 8.5 gm. and the albumin was said to be 6.1 gm. and the globulin 2.4 gm. In another the protein was 8.4 gm., the albumin 3.9 gm., and the globulin 4.5 gm. I should tend to believe the latter values. It seems to me that with the repeatedly high protein levels, one has to consider disease in the liver.

FIGURE 1.

CLINICAL DIAGNOSIS

Duodenal ulcer?
Splenic-vein thrombosis?

DR. EMERY'S DIAGNOSES

Duodenal ulcer.
Acute allergy.
Pressure on portal vein?

ANATOMICAL DIAGNOSIS

Tuberculosis of jejunum, ileum and regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr. Leland S. McKittrick operated on this man and was unable to find anything abnormal in the stomach or duodenum. Beginning about 10 cm. from the ligament of Treitz was the first of multiple constricting lesions of the small intestine. The largest lesions were in the proximal 25 cm. of the jejunum and this segment was resected (Fig. 1). The mesentery contained several enlarged nodes, and although the mesenteric fat did not extend very far over the intestine the diagnosis of regional enteritis was considered at operation. In most cases of regional enteritis the fat becomes extremely boggy and extends over the surface of the bowel. Here the fat was soft, not boggy, and the lesions were of a constricting nature, with a tendency to encircle the bowel. I was called to the operating room before resection and given the story of bleeding over a long period of time, and I therefore suggested that it might be a Kaposi's sarcoma involving the bowel. There were three or four lesions 2 to 3 mm. in diameter in the ileum, one of which was resected.

When the bowel was opened, the constricting lesions proved to be ulcerations (Fig. 2), and in the gross we thought that the best bet was a regional enteritis. We could not rule out tuberculosis or any other granulomatous process. The microscopic sections showed an acute and chronic process with granulomatous tubercle-like lesions and an occasional giant cell in both the base of the ulcer and the regional nodes. One large node was broken down and suggested caseation. Twenty-five years ago I am sure that most pathologists would have made a definite diagnosis of tuberculosis. Within recent years, however, since Crohn's[3] description of regional enteritis and because of the fact that we were unable to find any definite caseation on microscopic examination, we made a tentative diagnosis of regional enteritis. I was examining the slides this morning, not having seen them for a month or so, and the more I looked at them, the more I thought that the process was not characteristic of regional enteritis. I recalled that we had injected some of the material into a guinea pig, and although it was perhaps too early to autopsy the pig, we examined it and found a large node in the groin where the material had been injected. We therefore autopsied the pig and had no difficulty in finding tubercle bacilli in the node. The spleen and the iliac lymph nodes also showed tuberculosis.

Here then is a man who apparently was having chronic bleeding from tuberculosis over a long period of time. I do not recall seeing a similar case. Within recent years we have probably been leaning a little bit too far toward making the diagnosis of regional enteritis when we are confronted with these lesions and rarely consider tuberculosis. It is worth emphasizing the need of guinea-pig inoculation of material from all cases of suspected regional enteritis. The tuberculin test using a dilution of 1:50,000 was negative; it should have been repeated using stronger dilutions.

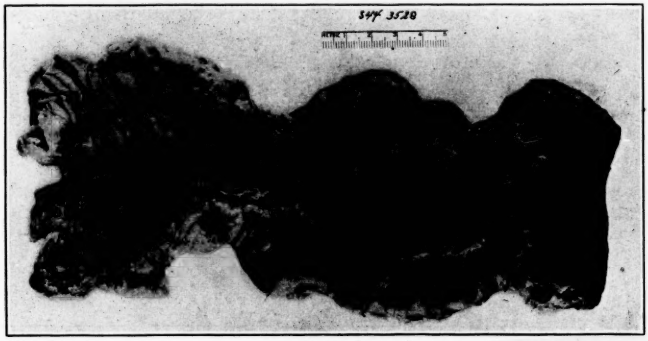

FIGURE 2.

DR. EMERY: How about the high serum globulin level?

DR. BUTLER: Dr. William Beckman entered a note in the record suggesting that a granulomatous disease might give a high serum globulin level.

DR. CASTLEMAN: The patient may have had tuberculosis involving the liver at the time of the operation. I do not believe that they examined the liver carefully at that time.

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CASE 30322

PRESENTATION OF CASE

A sixty-five-year-old gardener was admitted to the hospital complaining of a mass in the hypogastrium associated with anorexia and increasing weakness.

Fourteen months prior to admission the patient began to complain of anorexia, associated with nausea and vomiting occurring three or four hours after meals. He acquired a distaste for meat, fish and butter and limited his diet to milk, cereal, toast and an occasional egg. His weight, originally 248 pounds, fell to 177 pounds, and he became increasingly weak. Eight months prior to admission he developed extreme urgency and frequency, with nocturia ten to twelve times, dribbling and enuresis. The urinary stream was small and intermittent, requiring considerable straining. The urine had a foul odor. He noted a gradually increasing mass in the lower abdomen. Constipation, always a mild affliction, became severe, requiring Epsom salts or castor oil almost daily, but the stools appeared normal. Six months before entry he developed attacks of paroxysmal nocturnal dyspnea relieved by sitting up and by medication furnished by his physician. His ankles began to swell, and he developed dyspnea on exertion. At the time he was told that he had hypertension.

The patient claimed to have had rheumatic fever at the age of six, apparently without sequelae. Except for the fact that one sister had tuberculosis, the family history was noncontributory.

Physical examination revealed a pale, tired-appearing man. Venous pulsations were visible in the neck. The apical impulse was felt in the anterior axillary line. Rough apical and high-pitched aortic systolic murmurs were audible. There were frequent premature beats. At the base of the right lung the breath sounds were somewhat diminished and fine crackling rales were present. Over the lower third of the left chest posteriorly, and to a higher level in the left axilla, there were flatness to percussion, absent tactile fremitus and markedly diminished breath sounds. A nontender, symmetrical, smooth, cystlike mass measuring about 15 cm. in diameter was palpable in the hypogastrium, its upper border reaching a point 5 cm. below the umbilicus. The prostate was markedly enlarged, the right lobe being somewhat larger than the left, and a No. 20 Foley catheter could be passed only with difficulty. There was marked pitting edema of the legs up to the thighs and over the sacrum. The radial vessels were tortuous and very firm. The fundi showed advanced arteriosclerotic changes.

The blood pressure was 234 systolic, 84 diastolic. The temperature was 97.6°F., the pulse 70, and the respirations 20.

The red-cell count was 2,180,000, with 6.8 gm. of hemoglobin. The white-cell count was 4600, with 74 per cent neutrophils. A catheterized urine specimen revealed a specific gravity of 1.008 with a ++ test for albumin, and contained innumerable red cells, with 8 to 10 white cells and an occasional cast per high-power field. The serum nonprotein nitrogen was 142.5 mg. per 100 cc. The serum protein was 5.6 gm. per 100 cc., with an albumin-globulin ratio of 2.2. The fasting blood-sugar level was normal. The blood chloride was 109 milliequiv. per liter, and the carbon dioxide content 14.3 milliequiv. A blood Hinton test was negative.

Roentgenographic examination of the chest revealed a considerable amount of fluid in the left pleural cavity. The portions of the lungs unobscured by fluid appeared clear. The heart was not remarkable, but the left border was not distinctly demonstrated. A gastrointestinal series revealed some deformity of the duodenal cap but no definite ulcer crater. A barium enema was negative.

The bladder was catheterized, and 500 cc. of urine was withdrawn, following which the abdominal mass disappeared. Constant bladder drainage was instituted. The patient was also given digitalis and placed on a low-salt diet with a daily fluid intake of 2000 cc. orally. On this regime the sacral edema disappeared and the pleural effusion greatly diminished.

On the eleventh hospital day, on getting out of bed, the patient felt faint and everything "went black." He was put back to bed, where he complained of a severe persistent substernal pain. At that time the blood pressure was 160 systolic, 60 diastolic. An electrocardiogram revealed slight late inversion of T_1 and CF_4, a diphasic T_2, and an upright T_3, CF_2 and CF_4. This was thought to be consistent with either hypertensive or coronary heart disease, or both, but there was no evidence of recent infarction. A portable x-ray film of the chest was unsatisfactory. At that time there was slight tenderness of both calves but no ankle edema.

In the ensuing days, the patient continued to feel weak and faint, complained of persistent epigastric and substernal pain and began to hiccough. The blood nonprotein nitrogen, which had fallen to 87 mg. per 100 cc. on the fourteenth hospital day began to rise again, gradually reaching 125 mg. The urinary output diminished in spite of a daily fluid intake of more than 2500 cc. The urine had a specific gravity of 1.010, with a + to ++ test for albumin and innumerable white cells. The patient became increasingly lethargic and had constant episodes of retching. On the twenty-second hospital day the temperature rose to 100.2°F. Two days later, the breathing was loud, labored and bubbling, with bronchial breath sounds and numerous coarse rales throughout the chest. A pericardial friction rub and diastolic gallop rhythm appeared. The patient died on the twenty-fifth hospital day.

Differential Diagnosis

Dr. Marian Ropes: In this case, as is true in the cases of many patients of this age, a single diagnosis is not adequate to explain the picture. Several disease processes are apparent with manifestations that were typical, but other changes are hard to explain. I shall start with the more obvious ones.

The patient had hypertension and advanced arteriosclerosis. I assume that the heart disease and the resulting congestive failure were on that basis. In view of the story of rheumatic fever in the past it is impossible to rule out underlying rheumatic heart disease, although there is little evidence for this aside from the fact that an apical murmur of rough quality is more consistent with rheumatic than with arteriosclerotic heart disease; on the other hand, a high-pitched aortic murmur is equally consistent with rheumatic and arteriosclerotic heart disease. I believe, however, that the involvement of the heart was not the primary factor in the picture and was not directly related to the rest of it, except in so far as the severe congestive failure affected the other diseases present, such as renal failure. The pleural effusion on the left I assume to have been secondary to congestive failure. Unilateral effusion resulting from congestive failure occurs on the right side in the majority of cases, but on the left it is not uncommon. The possibility of underlying cancer or tuberculosis has to be considered in view of the rest of the picture.

One other definite fact is a disturbance of the genitourinary tract. The patient had definite prostatic hypertrophy. Not much information is given and it is difficult to determine whether it was benign hypertrophy or cancer of the prostate. I am assuming that it was the former. He surely had urinary infection, which was increased if not originally caused by the obstruction to the outflow of urine from the bladder. The sudden appearance of evidence of obstruction and infection at the same time, however, suggests that infection by the inflammatory reaction it caused at least played a role in the obstruction. Subsequently the patient developed renal failure, in which various factors must have played a role. There was an element of vascular nephritis, although it is difficult to determine the degree. The congestive failure presumably played some role, but without doubt the infection and the obstruction were the most important factors.

Beyond that, the picture becomes less definite. The onset of the illness, with gastrointestinal symptoms, and the subsequent loss of weight and weakness six months before evidence of cardiac failure and of renal disease suggest that these were not directly related to either cardiac failure or renal disease. They do suggest, however, the presence of some underlying disease, which I think was probably cancer, although tuberculosis must surely be kept in mind. The gastrointestinal symptoms

suggest either direct or indirect involvement of that tract.

This may be a good time to look at the gastrointestinal x-ray films. I judge that they show very little.

DR. MILFORD SCHULZ: They were negative.

DR. ROPES: There was no mass or evidence of extrinsic pressure?

DR. SCHULZ: Nothing.

DR. ROPES: Before attempting to put this together I should like to mention the attack of faintness and precordial pain on the eleventh hospital day. Various possibilities are suggested, such as coronary thrombosis, pulmonary infarct and hemorrhage. The subsequent course and findings, however, do not seem to support any of these. It is possible that the pain was caused by the pericarditis, of which there was evidence later in the form of a friction rub. This I assume was due to uremia. I also assume that the majority of the terminal symptoms were associated with the combination of cardiac failure and renal failure.

In attempting to sum this up, I am sure that this patient had hypertensive and arteriosclerotic heart disease with congestive failure and, terminally, pulmonary edema, presumably not related to the rest of the picture. I also believe that he had benign hypertrophy of the prostate. He certainly had a urinary-tract infection, with obstruction and renal failure, and died in uremia. I also believe that he had some underlying disease, but I find it hard to place, except that it involved the abdomen. It was probably a malignant tumor, the nature of which is not clear. I should guess that it arose primarily in the gastrointestinal tract, although there is little evidence for that. Possibly the genitourinary tract was involved.

DR. WILLIAM C. QUINBY: May I ask why you feel that there must have been some other cause? May not the renal difficulty have accounted for the digestive troubles in the beginning?

DR. ROPES: I thought that the digestive troubles and the loss of weight were out of proportion to the other evidence of renal abnormality.

DR. QUINBY: In my experience it is not uncommon to find an old gentleman coming in complaining of dyspepsia in whom the whole thing is due to an overfull bladder, which he does not realize is present. After the urinary tension is relieved, whether or not he gets well depends on the renal function. I really do not believe that one has to assume that this patient had a malignant tumor in the gastrointestinal tract.

CLINICAL DIAGNOSES

Arteriosclerotic and hypertensive heart disease.
Chronic vascular nephritis.
Uremia.
Prostatic hypertrophy.

DR. ROPES'S DIAGNOSES

Hypertensive and coronary heart disease, with congestive failure.
Pulmonary edema, terminal.
Benign prostatic hypertrophy.
Urinary-tract infection.
Uremia.
Malignant tumor of gastrointestinal tract?

ANATOMICAL DIAGNOSES

Prostatic hyperplasia.
Bronchopneumonia: left lower lobe.
Empyema, left.
Dilatation of bladder.
Hydroureter, bilateral.
Chronic pyelonephritis, slight.
Chronic vascular nephritis.
(Uremia.)
Cardiac hypertrophy.
Coronary sclerosis.
Rheumatic heart disease, with mitral and aortic stenosis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this man showed an enlarged heart, which weighed over 500 gm. There was no pericarditis. The coronary arteries were severely diseased, but no definite occlusion or infarction could be found. There was moderate rheumatic involvement of both the mitral and aortic valves, with slight calcareous aortic stenosis. In the left pleural cavity there was a liter of turbid, fibrinous fluid surrounding the lower lobe, which was completely solid; on section the consolidation was proved to be due to a confluent bronchopneumonia. I believe that the pneumonia and pleurisy began at the time that the patient had the severe chest pain.

Since there was no pericarditis, the friction rub must have been pleural in origin.

The kidneys together weighed 200 gm. and in gross showed a slight degree of vascular nephritis. Microscopically there were mild vascular changes and some evidence of pyelonephritis. The kidneys on examination would never lead one to believe that this patient had uremia with a nonprotein nitrogen of 140 mg. per 100 cc. He did, however, have some degree of pyelonephritis resulting from the large prostate, which had produced urinary retention. The bladder was markedly distended and trabeculated, and the ureters were slightly dilated.

I believe that a combination of factors produced death. He had a rather severe bronchopneumonia with early empyema, an enlarged decompensating heart and mildly diseased kidneys — all of which combined to put him into a mild state of uremia.

There were also a slightly thickened gall bladder and gallstones, which I do not believe played any role. The gastrointestinal tract was normal, and the enlarged bladder, as Dr. Quinby suggested, probably accounted for the digestive symptoms.

DR. ALLAN M. BUTLER: Would you agree that the prostatic obstruction was the factor in initiating the changes leading to this man's death?

DR. CASTLEMAN: Yes.

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THE MEDICAL OFFICER

Surgeon General Kirk[1] has said, "The human relationship of the doctor, patient and family cannot be laid aside with the donning of the uniform," and Colonel Herrman L. Blumgart,[2] addressing the members of the graduating class of the Harvard Medical School in December, 1943, emphasized this point when he quoted the legendary exclamation of the soldiers of Charles the Fifth: "We have no longer any fear to die, even if we should be wounded. Paré, our friend, is among us."

Yet such counsel is not always heeded, and there are, unfortunately, a small number of medical officers in the armed forces who have adopted in their care of the sick and wounded a degree of callousness well calculated to arouse just resentment. Such an attitude on the part of a medical officer, rare though it is, may well cause dislike not only of the physician involved but also of the service of which he is a part. It is possible that such an attitude is fostered by misinterpretation of the rarely heard admonishment, "Remember that you are an officer first, a doctor second." A high-ranking medical officer of the Army, — a man of great experience and with many years of service to his credit, — when asked if a doctor entering the service should adopt such a motto, replied, "If he does, Sir, he may make many enemies."

Every physician in civil life knows that a certain degree of detachment from a patient's plight must be developed if one is to retain one's objectivity. Every officer of the armed forces realizes that there are times — they may be few or they may be many — when his rank must come to the forefront of the situation. Every medical officer knows — as does his civilian counterpart — that there are times when one must crack down on a patient and perhaps be temporarily harsh. But it is well to remember that, as one medical officer of the Navy has said, "a sick or wounded fighting man has something that is just too big for him to handle, and unless he can repose his confidence and faith in you, there is but little to which he can look forward."

To physicians about to enter the armed services — indeed to those who already are medical officers — it might appropriately be said: see to it that neither the strain of battle nor the fatigue of long hours nor the tedium of inactivity nor the restiveness of being in a comparatively minor post nor anything else deter you from the just and proper care of the sick and wounded soldier. Is he — whether wounded, ill or malingering — fundamentally different from his counterpart in civil life? Only in these respects: he is far from home; he is doing something that he does not like; and he may well have been through living hell.

A hospital corpsman who landed with the first Marines on Guadalcanal closed his excellent discussion of this subject with these words: "I have my morphine and I have my tourniquet and my kit, and when I hear the cry 'Corpsman,' I creep up

on my belly hoping to God that the boy isn't dead before I get there and hoping to God I don't get killed before I reach him, and I give him the morphine and use my tourniquet if it's needed. And I ask you, doctor, What more is there left except encouragement and understanding and tact and the giving out of hope and the gaining of confidence?"

References

1. Kirk, N. T. A personal message from the Surgeon General. *Army Med. Bull.* **68**:248, 1943.
2. Blumgart, H. L. The doctor as medical officer in the armed forces. *Harvard Med. Alum. Bull.* **18**:78-81, 1944.

STRADDLING THE ISSUE

One interdiction, promulgated by those who watch sleeplessly over the Nation's welfare, that seems to have made little impression on the conscience of the country is the ruling of the War Food Administration relating to the use of heavy cream. Despite the apparent need for the conservation of our milk supply, this regulation, barring from retail sale, except on the prescription of a physician, cream containing more than 19 per cent of butterfat, seems to have acquired in the minds of many the status of an unpopular sumptuary law, possessing neither moral justification nor patriotic appeal.

An investigation has been made into the indispensability of heavy cream in the treatment of the sick, and no competent authority has been cited who is willing to champion any dietary need that cannot be met by the use of 19-per-cent cream with other fats. The Subcommittee on Medical Food Requirements of the Committee on Drugs and Medical Supplies of the National Research Council has denied the indispensability of this form of food; the Council on Foods and Nutrition of the American Medical Association has shown its use to be limited to the production of a ketogenic diet, and has admitted that this diet can be attained satisfactorily by the use of butter, salad oils and cream of the permissible fat content. Chiefs of various hospital services have disclaimed heavy cream as a necessary dietary adjunct; the Boston Medical Milk Commission has declared that its value in medical treatment is unimportant. And yet, according to the *Journal of the American Medical Association*,* available evidence indicates that during the past winter, in New York City alone, the equivalent of 500,000 quarts of milk went daily into heavy cream on doctors' prescriptions!

The *Journal of the American Medical Association* suggested a partial remedy for the situation, and the War Food Administration has, unfortunately, accepted the suggestion, which was put into effect as of August 1. The suggestion provides for the endorsement of the physician's prescription for heavy cream by such an official as the county health officer or the secretary of the county medical society; the amendment of the War Food Administration reconstructs the suggestion, leaving the approval of the physician's prescription to "the public health officer, or the secretary of the county medical society, of the municipality or county wherein such patient resides." First, the doctor is entrusted with an entirely superfluous responsibility, and then his medical colleague, or perhaps the local druggist, undertaker or carpenter, by virtue of his membership on the local board of health, is set as a watchdog over him!

This new gratuitous irritation seems to be a rather ill-considered way for an earnest, conservative governmental agency to avoid an issue. If there is a real need for the conservation of milk, — and we are constantly told that it exists, — and with heavy cream authoritatively declared to be a negligible factor in the treatment of illness, why, in all conscience, cannot this unnecessary luxury be withdrawn entirely from circulation instead of the doctor being again made the whipping boy, this time for cream to whip!

In Massachusetts, fortunately, this situation has undergone considerable amelioration through the farsightedness and energy of the state director of War Food Administration. This official, unable to obtain rescindment of the amendment, has obtained permission to place his own interpretation on its contents. By this interpretation a committee has been appointed to function in place of the variegated officers originally designated to approve the doctors' prescriptions.

Certainly a democracy at war that can accept selective service, tire confiscation, gasoline, fuel

*Editorial. Prescription of cream for the sick. *J. A. M. A.* **124**:511, 1944.

and food rationing, price administration, sales priorities, travel priorities, labor control and the highest taxes in its history can also do without one further luxury item — an item that millions of its people have never even seen. And while we are about it, if we have the courage to be about it, let us remove various other loads from the overburdened physician. Let us take away from him the burden of being considered the proper person to decide who is entitled to extra gasoline, for health reasons, or to extra fuel oil on the same basis. Where decisions of this nature are to be made on medical grounds, let medical panels be appointed to make them, without fear or favor. Let us try this time to rescue the doctor from the uncomfortable position that he occupied during the rousing days of prohibition.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

WHITMARSH — Willard F. Whitmarsh, M.D., of Bridgewater, died May 15. He was in his eightieth year.

Dr. Whitmarsh received his degree from Harvard Medical School in 1891. He was a member of the American Medical Association.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT

Needs of Public Health Service

The United States Public Health Service needs 322 physicians immediately. About 170 of these are required for assignment in the War Shipping Administration, for foreign shore duty with the United Nations Relief and Rehabilitation Administration and for sea and foreign shore duty in the United States Coast Guard. The remainder are needed for duties in the Hospital Division, foreign quarantine, tuberculosis control, venereal-disease control and other state control activities.

CORRESPONDENCE

NEW ARMY REGULATIONS FOR MIDDLESEX GRADUATES

To the Editor: I have been informed that interns, resident physicians and practicing physicians who are graduates of the Chicago Medical School or Middlesex University School of Medicine may be considered for commissions in the Army of the United States.

It is my understanding that such practicing physicians who desire consideration for appointment must be licensed to practice medicine and must have completed the regular medical course and have received the M.D. degree from their school, as attested by a letter from their dean; they must have experienced at least one year of rotating internship in a hospital approved for internship; they must hold membership in a local, county or district medical society or, if not meeting residence requirements for membership in any local society, they must submit evidence of actual engagement in the ethical practice of medicine through supporting letters from three practicing physicians who are graduates of approved medical schools and who are members of the local medical society where the applicant resides. In lieu of such letters, the applicants may submit a letter from the secretary of their local medical society attesting to the applicants' ethical practice of medicine and that they would be eligible to apply for membership in the society had they been in practice for a sufficient length of time.

Graduates of the Chicago Medical School or the Middlesex University School of Medicine in internship or resident training who desire consideration for appointment must be licensed to practice medicine and must have completed the regular medical course and have received the M.D. degree from their school, as attested by a letter from their dean; also they must submit a letter from their hospital vouching for their conduct while in training and indicating that they offer promise of competency in private practice. Such letters must be signed by at least three officers of the staff of the hospital concerned from among the following groups: chairman of the internship committee; superintendent of the hospital; chief-of-staff; and chief-of-staff of one of the special hospital services.

Reginald Fitz, M.D., *Massachusetts Chairman*
Procurement and Assignment for Physicians
319 Longwood Avenue
Boston 16

BOOK REVIEWS

To the Editor: I have just read with a great deal of interest the annual report of the librarian of the Boston Medical Library, which appeared in the June 22 issue of the *Journal*. I was particularly impressed with Dr. Viets's comments concerning the Book Review Department of the *Journal*, principally because I thoroughly approve of unsigned reviews, especially when it is obvious that the reviewers are carefully chosen.

We consider the book reviews in the *Journal* to be of unusually high quality, much above that of the average medical book review. Dr. Viets is to be congratulated for the consistently good reviews that appear in the *Journal*. There are far too few constructive criticisms of medical books, and the *Journal*, with its careful reviews, performs a real service not only to its readers but to authors.

T. A. Phillips
J. B. Lippincott Company
East Washington Square
Philadelphia 5

BOOK REVIEWS

Physiology of the Nervous System. By John F. Fulton, D.Phil., D.Sc. (Oxon.), S.B., M.D. Second edition, revised and reset. 8°, cloth, 614 pp., with 112 illustrations. London: Oxford University Press, 1943. $9.00.

In the five years that have passed since the publication of the first edition of this book, there have been many advances in knowledge of the physiology of the nervous system. Professor Fulton has taken cognizance of them and has rewritten his text, bringing it up to date. This monograph deals with the central nervous system, omitting the peripheral and sympathetic systems, except as they are related to the brain and spinal cord. Full accounts of the work of Dusser de Barenne on the sensory cortex and that of Ranson and many others on the deeper structures are given. In fact, no contribution of worth made in the last five years seems to have escaped the author, and this feature, as well as the soundness of his account of former work, makes the book of particular value as a reference volume.

The work on the biochemistry of synaptic transmission of the nerve impulse is fully considered. It is now known that acetylcholine is found in large amounts at the myoneural junction and that it effects the transmission of the nervous impulse across the synapse. This chemical, moreover, is controlled by enzymes — choline esterase, acting to destroy, and choline acetylase, a synthesizing agent. There is therefore a fine balance of a biochemical nature at the junction and, indeed, the same process or a similar process may go on at every point in the nervous system where two neurones are bridged by a synapse. These problems and others now in

the forefront of physiologic thought are fully elucidated in this new edition. Professor Fulton has called on many experts, particularly qualified in special fields, to aid him, and their material and the results of his own researches are integrated into each chapter by the author.

The reviewer believed that the first edition of this work was an outstanding contribution to the subject; his opinion is reinforced by the appearance of the second edition, so thoroughly revised and brought up to date. The book can be highly recommended to medical students, physicians and workers in laboratories and libraries. It is, indeed, a fundamental text that should find a place on the shelves of all medical libraries both public and private.

Lectures on Peace and War Orthopedic Surgery. Selected from the instructional courses presented at the eleventh annual assembly of the American Academy of Orthopaedic Surgeons, Chicago, January 17, 18, 19, 20 and 21, 1943. Edited by James E. M. Thomson, M.D. 4°, cloth, 322 pp., illustrated. Ann Arbor, Michigan: Edwards Brothers, Incorporated, 1943. $4.00.

Usually papers that are read in medical meetings do not have a prolonged appeal or arouse sufficient interest to warrant their separate printing in book form. But here is an exception. This book, a résumé of instructional courses in the orthopedic surgery of war given at the 1943 meeting of the American Academy of Orthopedic surgery, is timely and practical. Dr. James E. M. Thomson has edited the volume in a commendable manner. It is unfortunate that a few of the speakers failed to provide a synopsis of their talks. The book is well illustrated throughout. It is recommended as a valuable addition to the library of those interested in orthopedic surgery.

Gastro-Enterology (in three volumes). By Henry L. Bockus, M.D. Volume I: *The esophagus and stomach.* 4°, cloth, 831 pp., with 134 illustrations and 21 tables. Philadelphia and London: W. B. Saunders Company, 1943. $12.00.

This is an excellent book, probably the best on the subject in the last ten years. It is no simple compilation; the opinions are based on the author's large experience. It is well written, interesting and unusually complete, and unlike some books of its size it is not loaded with laboratory methods and types of treatment that are obsolete and have only historical value. It is fully illustrated. The x-ray illustrations are of especially high grade, being clear and definite and having a real purpose, which is a delightful contrast to some of the older textbooks. A great number of well-chosen references are found at the end of each chapter. Habits and fads in diagnosis and treatment are absent; in fact, there is a short section entitled "Avoidance of Enthusiasm for Certain Procedures."

Many controversial subjects, such as the etiology of peptic ulcer, the mechanism of its pain, its transformation into cancer, the value of gastroscopy and its relation to roentgen diagnosis, the relation of gastritis to peptic ulcer and cancer, the best antacids, the treatment of hematemesis by diets, transfusion and operation, and syphilis of the stomach, are treated with good judgment and skill.

The chapters on history taking, histology and physical examination are excellent. Modern methods of examination, such as "spot" roentgen films, gastroscopy, and peritoneoscopy, are freely used and discussed. The author uses the oral tube and fractional gastric analysis by choice, with eight or nine sets of analyses in each case over a two-hour period. Many gastroenterologists still prefer the nasal tube and will not agree that simple examination of fasting contents, with a single test of secretion, "has gradually gone into disuse." The microscopic examination of gastric contents covers ten pages with twenty-three illustrations. This seems rather elaborate in view of its lessened importance in recent years. The Einhorn string test is obsolete and uncertain and could be omitted, also the Woldman phenolphthalein test. The reader is referred to a textbook on laboratory technic for tests of the gastric contents. In a book of this size, simple tests for occult blood, lactic acid and so forth could be easily included.

Instead of a fifty-page chapter on roentgenologic examination of the stomach, excellent illustrations and comment are scattered through the book under different diseases. The chapter on gastritis is a great improvement on those written before the common use of the semiflexible gastroscope. The familiar forty-page chapter on gastric neuroses is conspicuous by its absence. There is a good discussion of pain, discomfort, anorexia, bloating and vomiting of nervous or reflex origin under the chapter on symptomatology. It is not quite clear why diaphragmatic hernia and esophageal hiatus hernia are described separately.

The discussion of peptic ulcer is very complete, taking about 40 per cent of the volume and covering etiology, diagnosis and medical and surgical treatment. Discussion of antacids is particularly useful. Perhaps the variability of magnesium trisilicate preparations should have been mentioned. The chapter on the complications of ulcer and the bad results that sometimes follow surgery are especially good. The illustrations of many types of gastric tumors are exceptional. Syphilis of the stomach is conservatively described.

All in all the book is of high quality and can be heartily recommended.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Medicine and the War. Edited by William H. Taliaferro, B.S., Ph.D. 8°, cloth, 193 pp., illustrated. Chicago: University of Chicago Press, 1944. $2.00.

This volume comprises a series of ten lectures by the members of the faculty of the Division of Biological Sciences, University of Chicago. These lectures were sponsored by the Charles Walgreen Foundation and although originally prepared for students, are applicable to the needs of the layman. They deal specifically with food in the war, chemotherapy, malaria, insects, disease, and modern transportation, shock and blood substitutes, aviation medicine, neurologic effects in cerebral injuries, psychiatry in the war, and chemical warfare.

The Health of Children in Occupied Europe. A pamphlet published under the auspices of the International Labour Office. 8°, paper, 37 pp. Montreal: International Labour Office, 1943. 25 cents.

This pamphlet provides a preliminary outline for the study of the effects of war on the health of children. The area covered comprises all the occupied countries of Europe.

NOTICES

HARVARD UNDERGRADUATE ASSEMBLY

The annual undergraduate assembly of the Harvard Medical School will be held in the amphitheater of Building E from 2:30 to 6:00 p.m. on Tuesday, August 29. The program will consist of eight student papers on original clinical and laboratory investigation, followed by an address at 5:00 p.m. by Dr. William T. Salter, professor of pharmacology, Yale University School of Medicine, whose subject will be "Drugs as Biologic Catalysts."

Medical students and physicians are cordially invited to attend.

AMERICAN CONGRESS OF PHYSICAL THERAPY

The twenty-third annual scientific and clinical session of the American Congress of Physical Therapy will be held September 6 to 9, inclusive, at the Hotel Statler, Cleveland. The annual instruction course will be held from 8:00 to 10:30 a.m. and from 1:00 to 2:00 p.m. during the days of September 6, 7 and 8. The scientific and clinical sessions will be given on the remaining portions of these days and evenings. All these sessions will be open to the members of the regular medical profession and their qualified aids.

For information concerning the instruction course and program of the convention proper, address the American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago 2.

(*Notices continued on page xvii*)